EDISON

Regeneus

Japan deal

Japan collaboration validates Progenza

Pharma & biotech

Regeneus has entered into a US$16.5m collaboration with AGC Asahi Glass (AGC) for manufacture of Progenza for the Japanese market. Regeneus and AGC have formed a 50:50 JV for clinical development and commercialisation of Progenza in Japan – we expect the JV to sub-license one or more partners to undertake clinical trials in a number of indications in Japan. We welcome the deal, which strengthens Regeneus's balance sheet and provides significant validation for the Progenza technology and IP. Our valuation of Regeneus increases to A$120m or A$0.57/share, with the AGC cash and larger addressable market in Japan partly offset by longer timelines and revised assumptions for CryoShot and Kvax.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (A$)	DPS (A$)	P/E (x)	Yield (%)
06/15	1.9	(6.6)	(0.03)	0.00	N/A	N/A
06/16	1.7	(3.6)	(0.02)	0.00	N/A	N/A
06/17e	11.7	6.1	0.03	0.00	5.7	N/A
06/18e	7.3	0.6	0.00	0.00	N/A	N/A

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

Deal details

AGC gains exclusive rights to manufacture Progenza for the Japanese market. Regeneus received US$5.5m upfront plus could earn up to US$11m of milestone payments. A JV was formed between the two companies for exclusive clinical development and commercialisation of Progenza in Japan for all clinical indications. Regeneus retains the rights to develop and manufacture Progenza for markets other than Japan. Regeneus's technology and experience expanding mammalian stem cell populations in culture will help accelerate AGC's entry into the manufacture of cell-based therapeutics in Japan.

Technology validation should open other doors

The AGC deal gives additional validation to the Progenza technology platform and IP, which were thoroughly reviewed during the due diligence process. This validation, combined with AGC's existing relationships with pharma and healthcare companies, should strengthen Regeneus's position as it engages with potential partners for clinical development and commercialisation of Progenza in Japan (as part of the JV) and in other markets.

Stronger balance sheet to fund development

Regeneus's cash balance was A$1.5m at 30 September 2016. The US$5.5m upfront payment, plus the prospect of additional milestone payments in the near term, gives Regeneus non-dilutive funding to support development of Progenza, its RGSH4K human cancer vaccine and its CryoShot and Kvax veterinary products.

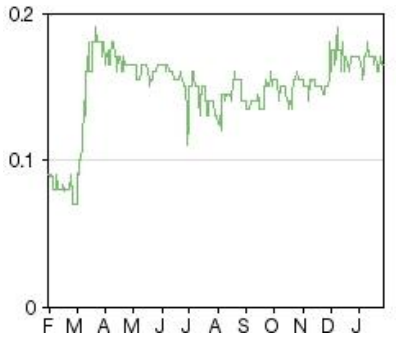
Valuation: Lifted to A$120m, A$0.57 per share

Our valuation of Regeneus increases to A$120m (vs A$108m) or A$0.57/share (vs A$0.52/share). Later forecast launch dates for Progenza (2022 in Japan and 2026 in other markets), plus more conservative assumptions for commercialisation of CryoShot and Kvax, partly offset the AGC deal cash.

27 January 2017

Price	**A$0.17**
Market cap	**A$35m**
	US$0.75/A$
Net cash (A$m) at 30 September 2016	1.5
Shares in issue	208.9m
Free float	67%
Code	RGS
Primary exchange	ASX
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	0.0	6.5	83.3
Rel (local)	(0.9)	1.2	61.9
52-week high/low		A$0.2	A$0.1

Business description

Regeneus is an Australia-based, clinical-stage regenerative medicine company developing innovative cell-based therapies for the human and animal health markets. It is focused on osteoarthritis and other musculoskeletal disorders, oncology and dermatology diseases.

Next events

Progenza STEP trial final results	Q2 CY17
First AGC milestone payments	2017
JV sublicenses clinical development partner in Japan	TBA

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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. In 2013, Regeneus acquired therapeutic cancer vaccine technology, which it is delivering for veterinary and human applications. Recent regulatory change in Japan offers a potential fast path to market for Progenza, its off-the-shelf human stem cell product, which is currently in a Phase I trial. Regeneus capitalised on this opportunity when it entered into a collaboration with AGC for the manufacture of Progenza in Japan and formed a joint venture for the development of Progenza for osteoarthritis and all other clinical indications in Japan. Regeneus's strategy is to focus on early-stage product development and to seek partners that will undertake the later stages of clinical development.

Valuation: A$120m or A$0.57 per share

We value Regeneus at A$120m, or A$0.57per share, based on a sum-of-the-parts DCF model, using a standard 12.5% discount rate. This represents fair value for the stock today, based on the potential development of multiple programmes including Progenza, CryoShot, Kvax, the RGSH4K human cancer vaccine and potential milestones under the AGC deal. Progenza is the key long-term value driver, with peak sales estimated at A$2.06bn, so clinical and regulatory progress over the next few years would significantly de-risk the product, which currently has a 30% probability of success in Japan and 15% in other markets.

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. Signing up AGC as a manufacturing partner for Progenza in Japan has provided significant validation of the commercial value of the company's technology; this should make it easier to sign clinical development partners, which represents near-term potential upside. Progress in developing additional indications for Progenza would also represent valuation upside.

Financials

Regeneus reported an operating loss of A$3.6m in FY16 (year ending June 2016), with net cash of A$2.6m used in operating activities in the period. Net cash at 30 June 2016 (end FY16) was A$0.5m, which had increased to A$1.5m at 30 September 2016 following the receipt of A$2.7m under the Australian government's R&D tax incentive scheme. The US$5.5m (~A$7.3m) upfront payment under the collaboration with AGC will significantly improve Regeneus's balance sheet. The agreement includes US$11m (~A$14.7m) of potential milestones – in our forecasts we assume that US$6m of these milestones will by the end of FY18. Regeneus had been tightly controlling expenditure as it awaited finalisation of the agreement with AGC. Given the improved balance sheet position and prospect of future milestone payments, we forecast R&D expenditure to grow by 20% in FY18 vs our previous forecasts of a 5% decline. We have assumed that the US$5.5m upfront payment will be booked as revenue in FY17, but note that a proportion of it could be reported as deferred revenue. We forecast Regeneus to report an operating profit and positive operating cash flow in both FY17 and FY18 vs our prior forecast losses. We forecast Regeneus to have A$5.8m of net cash at the end of FY18.

Regenerative medicines and cancer vaccines

Regeneus is developing and commercialising regenerative medicines and cancer vaccines. Its key regenerative medicines, Progenza (human) and CryoShot (veterinary), are based on a proprietary adipose (fat) derived allogeneic stem cell technology platform. The company is also developing the RGSH4K therapeutic human cancer vaccine, the Kvax canine cancer vaccine and products based on cell secretions for dermatology applications. The product portfolio (Exhibit 1) offers a mixture of near- and long-term opportunities, with a number of fast-track routes to market. Progenza and RGSH4K are currently in Phase I clinical studies, CryoShot is in a randomised pre-pivotal study in the US and Kvax is in a clinical study to generate efficacy data for marketing purposes.

Exhibit 1: Regeneus product portfolio

	Progenza	CryoShot	Human cancer vaccine	Kvax canine cancer vaccine	Secretions (topical)
Market	Human	Veterinary	Human	Veterinary	Human
Cell source/type	Allogeneic, adipose-derived	Allogeneic, adipose-derived	Autologous	Autologous	Allogeneic, adipose-derived
Cell production	Expanded cells, off the shelf	Expanded cells, off the shelf	Soluble proteins from patient's own tumour	Soluble proteins extracted from patients own tumour	Cell secretions from expanded cells
Mode of admin	Intra-articular	Intra-articular	Intradermal injection	sc injection	Topical
Primary indication	Osteoarthritis	Osteoarthritis	Solid tumours	Solid tumours, Osteosarcoma (dogs)	Acne
Regulatory status	Biologic requiring multiple safety and efficacy clinical studies for approval	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, Australia - 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 US, EU, Australia	US, EU, Australia	US, EU, Japan, Australia	US, EU, Australia	US, EU, Japan, Australia
Partner(s)	Licensed Japan manufacturing rights to AGC and formed JV for commercialising in Japan	Option agreement with unnamed top five veterinary pharma company	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 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 (MSCs) that have been multiplied in cell culture. The culture-expanded MSCs are frozen and stored in liquid nitrogen.

Progenza is initially being trialled 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.

A unique feature of Progenza 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. Evidence from animal studies indicates that the secretions provide an immediate anti-inflammatory effect when Progenza is injected into a diseased or damaged joint.

AGC deal brings cash and opens doors

Regeneus announced on 29 December 2016 that it had entered into a collaboration agreement with AGC Asahi Glass (AGC) for exclusive manufacture of Progenza stem cells for the Japanese market. Regeneus and AGC have also formed a 50:50 JV for clinical development and commercialisation of Progenza in Japan. The much-anticipated deal, which had taken 18 months to

finalise, brings cash (US$5.5m upfront and up to US$11m in milestones), a manufacturing solution and a partner that can open doors in Japan.

The intention is that the JV partners will license the Progenza technology to a third party, most likely a pharma company, which would be responsible for clinical trials, regulatory applications and commercial sales in Japan.

The thorough due diligence which AGC completed on the Progenza technology and IP, combined with AGC's existing relationships with pharma companies, means that Regeneus and the Regeneus Japan JV are well placed to attract partners for clinical development and commercialisation of Progenza, both in Japan and in global markets.

The clinical development of Progenza could extend well beyond the initial indication of osteoarthritis. For example, Mesoblast is developing allogeneic mesenchymal stem/precursor cell-based products in a range of indications including cardiovascular disease, lower back pain, diabetic kidney disease, graft vs host disease and rheumatoid arthritis. We see no reason why products based on the Progenza technology could not be developed for these same disease indications.

As an illustration of one of the indications that could potentially be targeted, we note that in December 2016 Regeneus announced a research collaboration with Macquarie University and the University of Adelaide to investigate the use of Progenza to treat chronic pain.

Progenza will be a key part of AGC's strategic plan

AGC is a Tokyo-headquartered multinational manufacturer that is part of the influential Mitsubishi group of companies, which are estimated to account for ~10% of Japan's GDP. AGC generated net sales in 2015 of ¥1,326bn and an operating profit of ¥71bn. Glass accounted for 52% of revenue, while the chemicals business segment, which includes the life sciences business unit, generated 22% of revenue.

As part of a 10-year strategic vision established in February 2016, AGC has designated life sciences as one of three high value-added strategic businesses where it will aim for high growth in targeted markets. It has made a number of acquisitions to help it achieve this goal.

On 19 December 2016, AGC acquired CMC Biologics (CMC), a Danish company with manufacturing facilities in Copenhagen in Denmark, and in Seattle and Berkeley in the US, for ~US$510m. CMC provides contract development and manufacturing organisation (CDMO) services for the manufacture of monoclonal antibodies, coagulation factors and other therapeutic proteins, including its proprietary CHEF1 expression system for production in mammalian cells. In September 2016, AGC acquired Biomeva, based in Heidelberg, Germany, undertakes contract manufacturing of biopharmaceuticals using microbial expression technology.

AGC already had existing facilities in Japan for the manufacture of biological pharmaceutical products. We believe that these facilities produce products such as monoclonal antibodies through microbial fermentation.

Progenza gives AGC a foothold in the regenerative medicine space through access to IP-protected regenerative medicine products. This is important strategically, given that Japan's Ministry of Economy, Trade and Industry has estimated that the domestic regenerative medicine market will be valued at ¥95bn in 2020 and at ¥1tn by 2030. This growth will be driven by new laws that took effect in Japan in November 2014, which allow for expedited conditional approval of regenerative medicine products on the basis of safety and early evidence that is predictive of efficacy. Conditional approval for a cell therapy would be valid for up to seven years, and use of the product could also benefit from national reimbursement of up to 70%. Full approval would be contingent on confirming efficacy and submitting the data to the PMDA within seven years of conditional approval.

Other Japanese companies are also diversifying into regenerative medicine

AGC is following a similar strategy to that being pursued by Fujifilm, which has established a regenerative medicine division to counteract stagnant demand for its office printing, digital cameras and photo printing equipment products. Fujifilm had grown its regenerative medicine division to 450 staff by mid-2016 through a number of strategic acquisitions.

Fujifilm bought US regenerative medicine company Cellular Dynamics for US$307m in 2015. In December 2016 Fujifilm announced it would acquire the Wako Pure Chemical Industries unit from Takeda for ¥155bn (US$1.31bn). Wako markets a range of laboratory reagents and specialty chemicals including reagents used in cell culture. In 2014 Fujifilm moved to majority ownership of Japan Tissue Engineering, which develops regenerative treatments for skin and cartilage.

Interestingly, in January 2017 Fujifilm entered an agreement with Australia-based Cynata giving it an option to develop and commercialise Cynata's induced pluripotent stem cell (iPSC) derived MSC product for graft versus host disease, which is unrelated to the osteoarthritis indication that Regeneus is targeting with Progenza.

Plenty of regenerative medicine deal activity in Japan

There have been a number of recent deals involving regenerative medicines in Japan, which show that these products can attract significant valuations.

In November 2016, Kolon Life Science of Korea entered into a licensing agreement with Mitsubishi Tanabe Pharma for the Japanese rights to Invossa, a cell-mediated gene therapy for degenerative osteoarthritis. Terms included US$24m upfront, plus US$410m in development, regulatory and sales milestones and a double-digit sales royalty. Mitsubishi Tanabe will proceed with Japanese clinical trials and regulatory filings. Invossa contains cultured non-transformed chondrocytes mixed with chondrocytes transformed to express transforming growth factor beta 1 (TGF-β1). Kolon has completed a positive Phase III in 156 patients with knee arthritis in Korea.

In January 2016 Athersys partnered with Helios to exclusively develop and commercialise its MultiStem cell therapy for ischemic stroke, plus up to two other indications, in Japan. The deal included US$15m upfront and up to US$225m in milestones plus double-digit royalties.

In July 2016 Takeda licensed from TiGenix the ex-US global right to Cx601, a suspension of allogeneic adipose-derived stem cells injected intralesionally for the treatment of complex perianal fistulas in patients with Crohn's disease. Terms included €25m upfront, up to €355m in milestones and double digit royalties on sales.

In February 2016 Astellas Pharma completed the US$379m acquisition of regenerative medicine company Ocata Therapeutics, which is developing cell-based therapies for eye diseases including age-related macular degeneration (AMD).

21st Century Cures Act expected to expedite market entry for regenerative medicines in the US

The 21st Century Cures Act, which was signed into law in the US in December 2016 by President Obama, will allow the US FDA to grant accelerated approval to regenerative medicine products, and will give the FDA wide discretion in creating new approaches to regenerative medicine. The new accelerated approval pathway allows certain regenerative medicine products to be designated as a "regenerative advanced therapy", which is defined as "cell therapy, therapeutic tissue engineering products, human cell and tissue products". To qualify for this pathway, the product must be aimed at a serious disease and have the potential to deal with currently unmet medical needs.

Similar to the existing accelerated approval pathway for drugs and biologics, the new pathway would allow a regenerative medicine product to be approved on the basis of surrogate or intermediate clinical trial endpoints such as imaging data or biomarkers in the blood rather than longer-term clinical outcomes.

Regenerative medicine products will still need to demonstrate safety and efficacy under the accelerated approval pathway, but the level of evidence required is less stringent than required for a full approval. This approach is more stringent than the conditional approval mechanism that is in place in Japan.

At this stage it is not clear whether or not an osteoarthritis indication for Progenza would satisfy the "serious disease" criterion, but some other potential indications such as graft vs host disease would be expected to qualify.

We revise our Progenza development timeline

Enrolment in the Phase I STEP (Safety, Tolerability and Efficacy of Progenza) trial of Progenza in patients with knee osteoarthritis was completed in April 2016. An interim review of safety data in May 2016 did not identify any safety concerns, and 12-month follow-up data are expected in Q2 CY17. While safety and tolerability is the primary outcome of the STEP trial, patients will also be monitored to assess the effect of Progenza on knee pain and function, quality of life, knee structures as assessed by MRI, and osteoarthritis biomarkers.

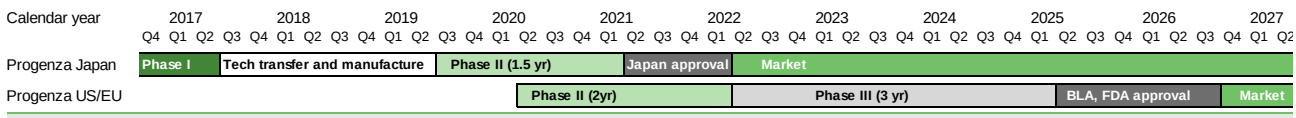
The next step will be a Phase II efficacy trial in Japan in patients with knee osteoarthritis; Regeneus's preference is for this trial to be conducted by a clinical development partner. Conditional approval in Japan requires demonstration of safety and data that are predictive of efficacy, but what efficacy evidence is required is not well defined. The trial design will be determined during discussions with the PMDA. It is not clear whether a randomised trial would be required, or whether improvements vs base line would be sufficient evidence. Likewise, the efficacy endpoints could potentially be pain and/or function three or six months after treatment or, alternatively, the regulator may want to see evidence of physical joint changes in the 12 months after treatment.

We assume that the JV or a clinical development partner would adopt the trial design with the minimum efficacy hurdles that were acceptable to the PMDA in order to maximise the likelihood that the clinical trial would report a positive result and support an application for conditional approval.

We assume that technology transfer and GMP manufacture of Progenza by AGC would take 2.5 years, enabling a Phase II trial in Japan to commence in Q3 CY19. Assuming the Japanese Phase II takes 18 months to complete (12 months to recruit, three months' follow-up, three months to report), results could be reported in Q1 CY21 with a potential market launch in early 2022.

At this stage in our forecasts we take a conservative approach and now assume that a separate Phase IIb trial will be conducted outside Japan to support Phase III efficacy studies in the US and Europe, with the Phase IIb study commencing in 2020 leading to a potential market launch in 2026, as shown in Exhibit 2.

Exhibit 2: Edison's assumed Progenza development timeline



Source: Edison Investment Research

We increase our estimate of the prevalence of KOA in Japan

With a manufacturing partner for Progenza in Japan now in place we have moved to a country-specific estimate of the prevalence of symptomatic knee osteoarthritis in Japan vs our prior global estimate of a 10% prevalence[1] in over 55 year olds. We have identified three epidemiology studies that reported the prevalence of symptomatic, radiologically confirmed (Kellgren-Lawrence grade 2-4) osteoarthritis of the knee ("symptomatic KOA"), which are summarised below.

- Muraki et al (2009)[2] in a survey of 2,282 people aged 60+ in three separate communities reported a prevalence of symptomatic KOA of 26.1%.
- Sudo et al (2008)[3] reported an incidence of 21.2% for symptomatic KOA in people over 65 in an examination of 598 inhabitants of a single Japanese village.
- In a study by Siozaki et al (1999)[4] in a prospective population-based epidemiological study in 1,463 individuals aged 54-79 years in a rural community in Japan, the prevalence of symptomatic, radiologically confirmed KOA (K-L grade 2-4) was 7.4%.

Averaging these three data points, we estimate that 18% of the Japanese population aged 55 or over has symptomatic, radiologically confirmed KOA, equivalent to 9.0 million people (vs our previous assumption of 10% and 5.0 million people).

Slow recruitment in CryoShot Canine pre-pivotal trial

CryoShot is an allogeneic (off-the-shelf) product containing MSCs derived from the fat tissue of donor animals and expanded in cell culture. Regeneus has entered an option agreement with an unnamed top five veterinary pharma company to develop CryoShot Canine. Regeneus and the partner are jointly funding a randomised pre-pivotal study in 80 client-owned dogs with arthritis, which commenced in November 2015 at the University of Pennsylvania School of Veterinary Medicine.

Recruitment of subjects in the trial has been slower than expected, presumably because fewer dogs than expected satisfied the enrolment criteria. Whereas recruitment had been expected to complete by the end of CY16, the trial is currently 50% recruited with 40 of the 80 dogs enrolled in the trial. Regeneus has not announced any plans to open a second recruitment site, but it now has the financial resources to do so if it chooses. However, at the current recruitment rate, we estimate that the trial is likely to be fully recruited in early CY18 and report results in Q2 CY18 vs our previous expectation of a Q2 CY17 report date.

At the completion of the trial the partner will have an option to exclusively license the CryoShot technology for canine applications; under the terms of the licence, Regeneus will receive an upfront fee, milestone payments and a royalty on sales. The results of the study will be used to finalise the design of a pivotal US FDA trial, which would be funded by the partner.

We assume that the pivotal trial will be a multicentre trial allowing recruitment to be much faster than the current single-centre, pre-pivotal trial. With the pivotal trial now assumed to begin in H2 CY18, we have delayed our forecast launch date for CryoShot in the US and Europe by a year to 2021 (Exhibit 3).

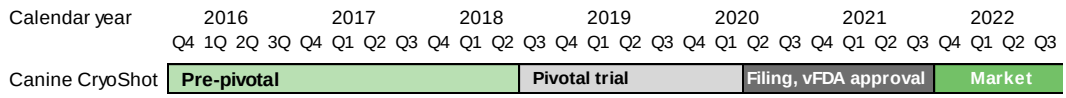
1 Heidari et al (2011) *Caspian J Intern Med*; 2(2):205-212.

2 Muraki et al (2009) *Osteoarthritis and Cartilage*; 17, 1137-1143. Table II

3 Sudo et al (2008) *J Orthop Sci*; 13(5):413-8. doi: 10.1007/s00776-008-1254-2

4 Siozaki et al (1999), *The Knee;* 6: 183-188; Table 3

Exhibit 3: Edison's assumed CryoShot development timeline



Source: Edison Investment Research

Therapeutic cancer vaccines

Regeneus has developed autologous cancer vaccines from technology licensed from the Kolling Institute of Medical Research. The technology 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.

RGSH4K human cancer vaccine

Regeneus initiated the ACTIVATE Phase I trial of its RGSH4K human therapeutic cancer vaccine in mid-2015. ACTIVATE is a single-centre, open-label, dose-escalating study of the safety and preliminary efficacy of the vaccine. The trial will recruit 21 patients with a range of advanced cancers. Recruitment had been anticipated to be completed in Q4 CY16, but the 2016 AGM presentation indicated that recruitment was expected to be completed in H1 CY17.

Recruitment of patients to bank tumour samples for preparation of the vaccine has gone well, but patients only receive RGSH4K injections when they reach end-stage disease after having exhausted all standard treatments, so the timing of subject dosing is difficult to predict.

Assuming that the Phase I trial reports results in 2018, an accelerated approval in the US under the 21st Century Cures Act could potentially be achieved in 2022 following completion of a Phase II trial. On the other hand, if a Phase III efficacy trial is required, then approval could be achieved in 2026. In our indicative valuation of RGSH4K we currently assume approval in 2024, the midpoint between these two scenarios.

Regeneus intends to explore the opportunity to combine RGSH4K with the immune checkpoint inhibitor (ICI) class of drugs. RGSH4K is designed to initiate an immune response, while the ICI drugs effectively "take the handbrake off" immune responses making them more potent, so the combination of the two approaches could potentially stimulate highly effective immune responses against cancer cells.

Regeneus has indicated that it is exploring partnering opportunities for RGSH4K in combination with ICIs. In our view, it is likely that efficacy trials would combine RGSH4K with an ICI such as Keytruda (pembrolizumab, Merck), Opdivo (BMS) or Tecentriq (Roche), or one of the ICI drugs that is currently in development.

RGSH4K uses a chemical modification of the patient's own tumour proteins to couple them to a bacterial adjuvant to make them more immunogenic. This relatively simple manufacturing process would be expected to translate to a low cost of manufacture for a personalised cancer vaccine.

A number of companies are already studying cancer vaccines in combination with ICI therapy. For example, Merck and Agenus are collaborating in a Phase II trial of Keytruda in combination with Agenus's Prophage autologous cancer vaccine in glioblastoma. Merck has also combined Keytruda with Genexine's cancer vaccine GX-188E in clinical trials in HPV-induced cancer. BMS is testing Opdivo with Bavarian Nordic's CV301 and Prostvac in non-small cell lung cancer and prostate cancer respectively, while Roche is investigating Tecentriq in combination with BioNTech's personalised cancer vaccine.

ICIs that are still in development are also being combined with cancer vaccines. For example, Merck and Pfizer are testing their PD-L1 drug avelumab alongside Transgene's TG4001 cancer vaccine, while AstraZeneca is combining the PD-L1 inhibitor durvalumab with a cancer vaccine from TapImmune in ovarian cancer.

Osteosarcoma trial suggests Kvax canine cancer vaccine improves survival

In addition to the RGSH4K human product, Regeneus is also developing a therapeutic cancer vaccine for use in dogs, known as Kvax. The company conducted a marketing study of Kvax 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. Thirteen dogs with osteosarcoma were treated with multiple doses of Kvax following amputation of the affected limb. The median progression-free interval (PFI) was 125 days and median overall survival (OS) was 182 days. The investigator concluded that Kvax was well tolerated and appears to confer improved PFI and OS compared to a historical control group.

Regeneus is currently recruiting subjects in a separate trial of Kvax in 45 dogs with lymphoma, which began in November 2015. The double-blind, placebo-controlled trial, being conducted by veterinary oncologists at the Small Animal Specialist Hospital in Sydney, Australia, will use Kvax together with chemotherapy to seek to extend remission times in dogs that initially respond to chemotherapy. Lymphoma is the most commonly treated cancer in dogs; remission typically lasts eight to 10 months with chemotherapy, with a median survival of about one year.

Regeneus has been advised by the Center for Veterinary Biologics at the US Department of Agriculture that it can commercialise Kvax in the US without obtaining specific regulatory approval. We do not expect the product to be launched commercially until further efficacy data are available to support marketing efforts.

Cell secretions for inflammatory conditions

Regeneus has developed technology for topical treatment of inflammatory skin conditions such as acne and wound healing. The technologies harness the anti-inflammatory properties of the secretions released by MSCs during cell culture. The company has partnered with CSIRO on scale-up manufacturing and developing the capability to produce cell secretions at commercial scale and plans to conduct further preclinical and clinical testing of the secretions-based technologies.

Valuation

Our valuation of Regeneus has increased to A$120m (vs A$108m), or A$0.57/share (vs A$0.52/share). We have included upfront and milestone payments from the AGC Asahi Glass collaboration agreement and raised the estimated addressable market for Progenza in Japan, partly offset by later forecast launch dates for Progenza, and CryoShot and, and by a change to more conservative effective royalty rate assumptions for CryoShot and Kvax. The main changes to our forecasts are described below. We have:

1. included the US$5.5m upfront payment and risk-adjusted milestone payments totalling US$11m from AGC. We assume that the milestones will become payable over FY17-21, with a greater weighting to the near term;
2. delayed forecast market launch for Progenza in Japan by two years to 2022 to allow time for transfer of Progenza manufacturing technology to AGC before initiating a clinical trial in Japan;

3. separated out our forecasts for Progenza in Japan from forecast sales in the US, EU and Australia, and for the first time applied a higher 30% likelihood of approval in Japan (vs 15% in other territories) to reflect the potential for conditional approval of regenerative medicines in Japan based on clinical trials that are predictive of efficacy. We have also reduced Regeneus's economic interest in Progenza in Japan to a 10% net royalty (vs 20%) to reflect the 50:50 JV with AGC in Japan covering osteoarthritis and all other clinical indications and increased the estimated prevalence of symptomatic KOA in over 55s to 18% (vs 10%);
4. delayed forecast market launch for Progenza outside Japan by two years to 2026 on the assumption that Phase II trials in other territories will not begin until 2020, as illustrated in Exhibit 2 (the higher KOA prevalence estimate in Japan and the extra two years of 3% market growth before peak sales are reached ex-Japan sees Progenza peak global sales increase to A$2.06bn [vs A$1.75bn]);
5. for the veterinary products CryoShot and Kvax, we have changed to a more conservative effective royalty rate of 20% (vs 30%) on the assumption that Regeneus will pursue a lower-risk out-licencing strategy rather than a higher-risk (but potentially more profitable) joint development strategy;
6. delayed forecast launch of CryoShot in the US and Europe by one year to 2021 (Exhibit 3);
7. removed the assumption that Regeneus would generate modest sales of Kvax in FY17-18 while marketing studies are underway (previously 85% likelihood). We now assume that Kvax commercial sales will begin in 2019 after marketing studies are completed, with the likelihood of those sales unchanged at 40%; and
8. reallocated R&D expenditure so that the majority is allocated to development of Progenza, reducing forecast R&D expenditure on CryoShot and Kvax.

Our sum-of-the-parts DCF valuation model is summarised in Exhibit 4, with key assumptions shown in Exhibit 5.

Exhibit 4: Regeneus valuation model

Product	Setting	Region	Status	Launch	NPV (A$m)	Peak sales (A$m)	Probability of success	Economic interest	rNPV (A$m)	rNPV per share (A$)
Progenza	Human - OA	Japan	Phase I	2022	109.1	504	30%	Royalty (10%)	30.2	0.14
Progenza	Human - OA	Australia/ EU/US	Phase I	2026	286.6	1,558	15%	Royalty (20%)	35.6	0.17
Human cancer vaccine	Solid tumours	WW	Phase I	2024	91.1	500	15%	13% net royalties	12.8	0.06
CryoShot	Animal - OA	Australia	Pre-registration field trials	2012	14.2	7	30-100%	Operating profit (40%-60%)	4.2	0.02
CryoShot	Animal - OA	EU	Pre-pivotal studies	2021	18.4	46	30%	Royalty (20%)	5.1	0.02
CryoShot	Animal - OA	US	Pre-pivotal studies	2021	24.5	55	30%	Royalty (20%)	6.8	0.03
Kvax canine vaccine	Dog cancer	WW	Marketing studies	2016 (Aus); 2019	23.3	43*	85%	Royalty (20%)	9.0	0.04
AGC upfront & milestones		Japan			18.3		30-95%		15.5	0.07
Portfolio total					585.7				119.2	0.57
Net cash (at 30 June 2016)									0.5	
Overall valuation									119.7	0.57

Source: Edison Investment Research. Note: *Incorrect value of A$35m was included in Exhibit 1 of Edison's previous report dated September 2016.

Our valuation model applies a standard 12.5% discount rate and includes net cash of A$0.5m at end June 2016. We assume that product sales reach peak market share six years after launch, grow in line with market for the next four years and then decline at 10% per year. For simplicity, we do not include upfront and milestone payments from any potential future licensing deals that have

not yet been signed 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. Risk adjustments would unwind as programmes advance through clinical studies, gain regulatory approvals and secure commercial partners, etc.

Exhibit 5: Regeneus valuation assumptions

Product	Setting	Region	Status	Key assumptions
Progenza	Human - OA	Japan	Phase I	Prevalence ~18% of >55yrs; 10% suitable candidates for treatment; 10% Progenza peak market share (2028; 6 yrs to peak); A$5,000 per procedure; 50:50 JV with AGC for Japan.
Progenza	Human - OA	Australia/EU/US	Phase I	Prevalence ~10% of >55yrs in all regions; 10% suitable candidates for treatment; 10% PRG peak market share (2031; 6 yrs to peak); A$5,000 per procedure (A$3,750 in EU).
Human cancer vaccine	Solid tumours	WW	Phase I	$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 of probability (100% near-term to 30% post-2020).
CryoShot	Animal - OA	EU	Pre-pivotal studies	~90,000 small animal vet practitioners; peak penetration in 2026, with 3% use CryoShot, 50x per year, at A$250 per dose; 30% probability with studies/partners to complete.
CryoShot	Animal - OA	USA	Pre-pivotal studies	~50,000 small animal vet practitioners; peak penetration in 2026, 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 2024 (=21,600 Kvax treatments); A$2,000 per treatment course; 40% probability with studies/partners to complete.
AGC upfront & milestones		Japan		US$5.5m upfront; plus US$11m milestones, assume payable over FY17-FY21, risked at 30-90%.

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. Signing up AGC as a manufacturing partner for Progenza in Japan has provided significant validation of the commercial value of the company's technology; this should make it easier to sign clinical development partners, which represents near-term potential upside.

Progenza could potentially be developed for a range of disease indications. At present we include only the single osteoarthritis indication in our valuation model, so progress in developing additional indications or licensing deals that include additional indications for Progenza represent potential sources of upside to our valuation.

Financials

Regeneus reported an operating loss of A$3.6m in FY16 (year ending June 2016), with net cash of A$2.6m used in operating activities in the period. Quarterly operating cash outflow in Q117 (three months ending September 2016) was A$1.7m (excluding the R&D tax incentive). Cash at 30 June 2016 was A$0.5m, which had increased to A$1.5m at 30 September 2016 following the receipt of A$2.7m under the Australian government's R&D tax incentive scheme. The US$5.5m (~A$7.3m) upfront payment under the collaboration with AGC will significantly improve Regeneus's balance sheet. The agreement includes US$11m of potential milestones – in our forecasts we assume that US$6m of these milestones will be received by the end of FY18.

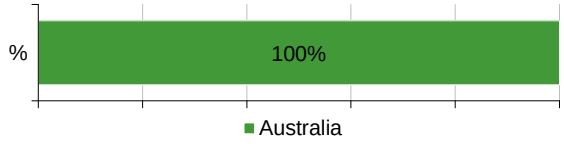
Regeneus had been tightly controlling expenditure as it awaited finalisation of the agreement with AGC. Given the improved balance sheet position and prospect of future milestone payments, we now forecast R&D expenditure to grow by 20% in FY18 vs our previous forecast of a 5% decline. We expect R&D spend to grow by a further 15% in FY19 (forecasts not shown) and have increased forecast SG&A expenses in FY18 by 8%. We have assumed that the US$5.5m upfront payment will

be booked as revenue in FY17, but note that a proportion could be deferred to future years. We now forecast Regeneus to report an operating profit and positive operating cash flow in both FY17 and FY18 vs our prior forecast losses. We forecast Regeneus to have A$5.8m of net cash at the end of FY18.

Exhibit 6: Financial summary

A$'000s	2014	2015	2016	2017e	2018e
Year end 30 June	AASB	AASB	AASB	AASB	AASB
PROFIT & LOSS					
Revenue	2,003	1,900	1,735	11,698	7,303
Cost of Sales	(621)	(915)	(292)	(240)	(363)
Gross Profit	1,381	985	1,444	11,457	6,940
R&D expenses	(5,758)	(4,945)	(4,309)	(4,525)	(5,430)
SG&A expenses	(6,756)	(6,250)	(3,578)	(3,564)	(3,903)
EBITDA	(10,800)	(9,805)	(6,092)	3,615	(1,870)
Operating Profit (before GW and except.)	(11,118)	(10,191)	(6,428)	3,375	(2,390)
Intangible Amortisation	(16)	(19)	(15)	(7)	(3)
Exceptionals	0	0	0	0	0
Other (includes R&D tax credit)	3,767	3,418	2,747	2,715	2,986
Operating Profit	(7,367)	(6,792)	(3,696)	6,083	594
Net Interest	(157)	186	122	(20)	(20)
Profit Before Tax (norm)	(7,507)	(6,588)	(3,559)	6,070	577
Profit Before Tax (IFRS)	(7,523)	(6,607)	(3,574)	6,063	574
Tax benefit	0	0	0	0	0
Profit After Tax (norm)	(7,507)	(6,588)	(3,559)	6,070	577
Profit After Tax (IFRS)	(7,523)	(6,607)	(3,574)	6,063	574
Average Number of Shares Outstanding (m)	166.5	208.9	208.9	209.9	210.9
EPS - normalised (A$)	(0.05)	(0.03)	(0.02)	0.03	0.00
EPS - IFRS (A$)	(0.05)	(0.03)	(0.02)	0.03	0.00
Dividend per share (A$)	0.00	0.00	0.00	0.00	0.00
BALANCE SHEET					
Fixed Assets	3,170	2,451	2,432	3,378	3,613
Intangible Assets	30	26	11	27	52
Tangible Assets	1,362	892	802	1,731	1,942
Investments	1,778	1,533	1,619	1,619	1,619
Current Assets	7,089	7,128	3,503	8,712	9,145
Stocks	206	99	30	112	169
Debtors	134	67	22	22	22
Cash	2,635	3,013	529	5,673	5,778
Other	4,114	3,950	2,922	2,905	3,176
Current Liabilities	(1,698)	(1,260)	(1,006)	(1,006)	(1,006)
Creditors	(921)	(781)	(906)	(906)	(906)
Short term borrowings	0	0	0	0	0
Other	(777)	(478)	(99)	(99)	(99)
Long Term Liabilities	(253)	(48)	(144)	(144)	(144)
Long term borrowings	0	0	0	0	0
Other long term liabilities	(253)	(48)	(144)	(144)	(144)
Net Assets	8,308	8,272	4,785	10,939	11,608
CASH FLOW					
Operating Cash Flow	(6,239)	(5,923)	(2,253)	6,337	863
Net Interest	0	0	0	0	0
Tax	0	0	0	0	0
Capex	(1,176)	(208)	(250)	(1,192)	(757)
Acquisitions/disposals	0	8	19	0	0
Financing	10,209	6,168	0	0	0
Dividends	0	0	0	0	0
Other	4,900	0	0	0	0
Net Cash Flow	7,694	45	(2,484)	5,144	105
Opening net debt/(cash)	4,366	(2,635)	(3,013)	(529)	(5,673)
HP finance leases initiated	0	0	0	0	0
Other	(693)	333	0	0	0
Closing net debt/(cash)	(2,635)	(3,013)	(529)	(5,673)	(5,778)

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	

Management team

CEO: John Martin	Chairman: Dr Roger Aston
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.	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 UK, 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, he 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%

Companies named in this report

Mesoblast (ASX:MSB), Cynata (ASX:CYP), AGC Asahi Glass (TYO:5201), Fujifilm (TYO:4901), Takeda Pharmaceutical (TYO:4502), Kolon Life Sciences (KOSDAQ:102940), Mitsubishi Tanabe Pharma (TYO:4508), Chugai Pharmaceuticals (TYO:4519), Athersys (NASDAQ:ATHX), Astellas Pharma (TYO:4503)