EDISON

TxCell

CAR Treg update

Humanised CAR Tregs are a key step forward

Pharma & biotech

TxCell has announced it has a promising humanised CAR-Treg product that can be developed to control graft rejection in solid organ transplant. A trial is planned to start in late 2018. CAR Tregs offer a powerful and versatile new approach to immune system disorders; multiple sclerosis, lupus nephritis and the skin disorder bullous pemphigoid are also targets. TxCell had cash of €8.68m on 30 June. The indicative market cap has been rebased onto CAR Treg indications and is now €84.4m, formerly €74m.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/15	0.92	(10.78)	(88)	0.0	N/A	N/A
12/16	0.15	(12.73)	(98)	0.0	N/A	N/A
12/17e	0.26	(9.14)	(43)	0.0	N/A	N/A
12/18e	0.25	(11.43)	(44)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments. Share issues in 2016 and 2017 reduce EPS.

Focus on CAR Treg with four preclinical projects

TxCell is clearly set on being the leading CAR Treg company based on ENTrIA technology development. The ENTrIA platform uses chimeric antigen receptor (CAR) technology similar to that in the CAR T-cell cancer area. Developing a humanised CAR Treg is an important step as long-term control of chronic diseases may need repeat dosing. A granted European patent (licensed globally in June 2016) offers broad protection. CAR Treg trials are planned from late 2018 with solid organ transplant rejection as a lead indication. This is based on an academic collaboration and new humanised CAR Treg. Other indications are lupus nephritis, bullous pemphigoid (skin) and multiple sclerosis. We expect ENTrIA to be an excellent basis for partnering and technology licensing.

Financing and funding: costs €13m, cash €14.5m

TxCell estimates 2017 cash use at €13m including €2m to Trizell in late 2017. Cash on 30 June was €8.68m after the rights funding in February 2017, and pre-selling of tax credits to advance the cash flows. The rights warrants will yield €10.8m if exercised at €2.60 in February 2018 adding 4.1m shares. However, they are currently out of the money so other funding may be needed.

Valuation: CAR Treg basis, re-based to €84.4m

Edison has developed value estimates for the four CAR Treg indications. Transplant is the best defined and now valued tentatively on a DCF basis at €53m based on lung transplant probability of 12.5% and adding kidney at 7.5%. Other indications retain their nominal values as less defined. Ovasave, now on hold, has had its value reduced from a calculated €84m, to a nominal €20m as future cash flows are now uncertain. These changes alter the portfolio value to €130m from €154m. Costs have been reduced and are now forecast in detail to 2021 when potential CAR Treg partnering may occur, if not sooner. The new indicative valuation is €84.4m, formerly €74m. This may equate to a diluted 2018 value of about €3 per share, formerly €2.83/share, noting that additional share dilution from 2019 is likely.

9 October 2017

Price	**€1.67**
Market cap	**€34m**
Cash (€m) at 30 June 2017	8.7
Shares in issue (as of 27 September)	21m
Free float	59.45%
Code	TXCL
Primary exchange	Euronext Paris
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(2.9)	(15.2)	(39.9)
Rel (local)	(7.4)	(18.8)	(50.1)
52-week high/low		€2.8	€1.4

Business description

TxCell is developing regulatory T-cell therapies against autoimmune and inflammatory disorders. It is now focused on a novel CAR Treg technology platform. A clinical trial in transplantation may start in late 2018.

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Edison profile page

Taking the lead in Treg therapy

TxCell is one of the few companies focusing on regulatory T-cell therapy (Tregs) for autoimmune and inflammatory indications. The Treg area is underdeveloped and TxCell offers a rare investment opportunity, targeting transplant and major autoimmune indications. Tregs have very powerful control functions in the immune system and can control adverse immune responses (Singer et al (2014). The area is gaining increased interest with Novartis in an academic collaboration on a new clinical trial in Graft vs Host Disease. TxCell has a big advantage in Tregs as it is using CAR-T technology to improve the efficacy of Treg therapy. Additional information on Tregs, market sizes and the immune system is contained the note of February 2017.

TxCell's current Treg pipeline is

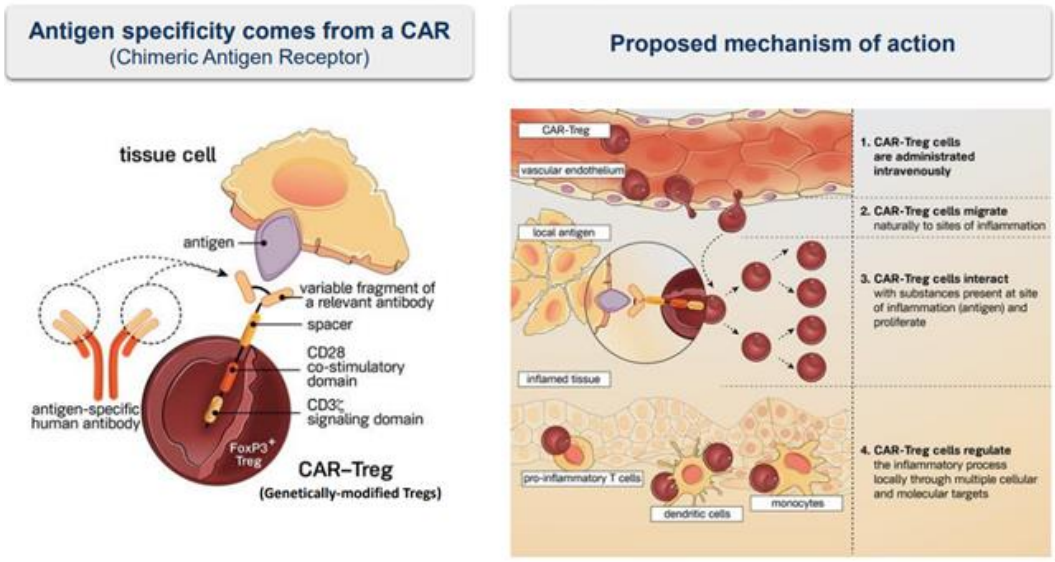
- Transplant
- Bullous pemphigoid (BP)
- Multiple sclerosis (MS)
- Lupus nephritis (LN)

The Phase II product, Ovasave, based on the earlier ASTrIA platform is on hold. Its manufacturing process has been optimised. TxCell will integrate know-how and intellectual property from the ASTrIA platform into its active CAR Treg projects. TxCell continues to explore licensing opportunities for its technologies and products including Ovasave.

CAR Tregs: A new area owned by TxCell

TxCell's CAR Treg platform offers flexible, powerful and precise targeting to any antigen and the transformed cells selected. The basics of CAR design, a fast-evolving field in the cancer space, are reviewed in Sadelain et al (2013) and also in the Edison report on T-cell cancer therapies. Exhibit 1 shows an overview.

Exhibit 1: CAR Treg technology and mode of action



Source: TxCell 22 Sept 2017 Corporate Presentation

CAR Tregs use an antibody fragment as a receptor to target Tregs to specific cell types or locations – like a transplanted organ. In the first generation, these antibody fragments were derived from

mouse antibodies which are easier to generate. However, these often are immunogenic so can only be used once as the immune system recognises and destroys them on subsequent use. As the antibody targeting domain of the CAR Treg is humanised, repeat doses of humanised Tregs can be given. The process involves harvesting patient cells, sending to a manufacturing facility, transfecting with virus and after culture and testing, returning to the patient for infusion. This process is accepted by regulatory authorities. TxCell has an agreement with Lentigen Technology for supply of the lentivirus vector used. A manufacturing CMO will be appointed. A clinical proof-of-concept study in transplantation is planned by TxCell to reach the clinic by late 2018 – this will be the first CAR Treg clinical study and could give validation of the CAR Treg concept by H12020.

The concept of CAR Tregs was published in a patent in 2008 by the Weizmann Institute of Sciences, Israel, EP2126054. This patent has been granted by the European Patent Agency and was licensed by TxCell in June 2016. It is in process in the US. This patent gives broad coverage. To provide further layers of extended protection, TxCell is developing other CAR Treg intellectual property, in the molecular technologies used and in manufacturing and processing technologies.

CAR Treg projects

Tregs are used by the immune system to control other immune cells, like CD8+ killer T-cells, to prevent them attacking normal tissues or generating toxic levels of cytokine signalling molecules to attract and activate other immune cells. It is assumed that CAR Tregs will enable immune disorders to be controlled without the use of toxic drugs. TxCell is developing CAR Tregs that recognise a specific antigen trigger. This can be a self- recognition antigen, like HLA (crucial for tissue matching in type, in transplantation), or a natural protein, perhaps as in multiple sclerosis. When the CAR Treg is activated by the signal, it will limit the activity of any active immune cells in the neighbourhood so down-regulating the immune response.

Exhibit 2: Selected Treg indications

Indication	Comments and description
Graft vs Host Disease	GvHD occurs in about 37% of patients within a year of an allogeneic stem cell transplants used to treat and ideally cure a haematological cancer (Arai et al (2016)). Done to cure haematological cancers if a patient enters remission. The patient's immune system is destroyed with chemotherapy and radiation. A donor bone marrow graft is given to regenerate the immune system. However, this can lead to GvHD. Jacobsohn and Vogelsang (2007) noted 5,500 cases of GvHD out of 13,700 stem cell transplants in 2003. It also occurs, although very rare, if T-cells contained within a transplanted solid organ recognise the host as foreign and attack.
Type 1 diabetes (T1D)	Relatively uncommon autoimmune disease where the insulin-producing cells of the pancreas are attacked and destroyed. Patients lead normal lives but need to inject insulin and are prone to long-term diabetic complications and dietary restrictions. Often manifests in adolescence but can occur in later life. No current TxCell project disclosed but possible target
Lupus nephritis	Lupus nephritis is a particularly severe and potentially fatal complication of lupus, the systemic chronic inflammatory disease. Some patients progress to end-stage renal disease, which can only be treated through dialysis and transplant.
Multiple sclerosis	This is an autoimmune disease in which the immune system attacks the insulating fatty myelin sheaths around the nerve fibres in the central nervous system. This means that the nerves progressively lose the ability to transmit signals effectively. The condition is chronic and progressive. Current therapies aim to control the immune system but can only slow disease progression.
Bullous pemphigoid	Bullous pemphigoid is a rare chronic skin inflammation where the lower layers of the skin are attacked by the immune system causing blistering. The condition can cause dehydration, which can be fatal. It is treated with steroids.
Organ transplant	This is the transplant of a whole organ. The commonest such operation is kidney followed by liver, lung and heart. Kidney donors can be living family members but most donors are deceased. Other transplants are more complex and need deceased donors. Rejection is a major issue controlled for life with drugs. Rejection can be acute and occur quickly driven by CD8+ T-cells or late and driven by antibodies. The rate of first acute rejection episodes in kidney transplants is about 10% after 12 months, 15% after three years and about 17% after five years. Only a few percent of grafts fail within 90 days of transplantation. Late-stage graft failure rates have been falling. The usual measure takes patients who have survived for one year with no problems and uses this cohort to assess half-life. Patients who have early problems tend to have short graft survival. On this basis, grafts from deceased donors had a half-life of 12.5 years and from living donors there was a half-life of 15.3 years. Note that GvHD from T-cells carried in a donated organ is rare.

Source: Edison Investment Research

Commercial potential Treg competitors

Industrial competitors are limited and many are not in the CAR Treg area but instead use either general Treg populations or sorted polyclonal Tregs against a target like an allograft (usually bone-marrow). Others are using mesenchymal or adipose stem cells. Exhibit 3 summarises projects.

Exhibit 3: Commercial Treg and other cell types in clinical developments

Company	Type and Indication	Trial number	Patients	Reporting	Comments
Mesoblast (Australia)	Phase III paediatric GvHD using Remestemcel-L	NCT02336230	60	Q417	The dose is eight doses of at 2m cells /kg. Doses are given between 3 and 5 days apart over four weeks.
Novartis	Pilot study in kidney transplant patients	NCT03284242	12	"Jan 17"	Autologous cultured Tregs given to patients using Zortress (Everolimus) as immunosuppressive therapy
ILTOO Pharma (France)	Open-label Phase II	NCT01988506	132	H117	12 autoimmune and auto-inflammatory diseases.
	Phase II Type 1 diabetes,	NCT02411253	138	Late 2017	Recently diagnosed, trial still recruiting but one year follow up
	Phase II in lupus	NCT02955615	100	Q118	Trial still recruiting, 12-week follow-up
Miltenyi Biotec Prometheus Labs	Phase I Tregs plus Low-Dose IL-2 in GvHD	NCT01937468	25	Q418	Led by Dana-Farber. Uses Treg enriched cells in patients with chronic GvHD after stem cell transplant
Caladrius Biosciences (US)	Phase II adolescent Type I diabetes	NCT02691247	120	2019	Autologous expanded Treg project: there are three dose arms "low" and "high" plus control. There is a one-year follow-up.
TiGenix	Phase III data with fistula in Crohn's disease	Positive outcome	212	2016	Not a Treg therapy but uses expanded adipose stem cells to help heal complex perianal fistulas. 120m dose. EMA opinion late 17.
Targazyme with MD Andersen	GvHD	NCT02423915	47	Mid-2019	A dose of 2.1x107 Tregs/kg is envisaged. The cells are modified before the graft by enzymic addition of fucose (a sugar)..

Source: Edison Investment Research based on clinicaltrials.org. Note: These are not antigen-specific.

The main new development project is a pilot study at the University of Kentucky with Novartis as a collaborator. This is enrolling 12 patients undergoing a kidney transplant. Tregs will be harvested, cultured and infused. The patients will use Zortress (Everolimus) as immunosuppressive therapy. These are unmodified Tregs and the study is small. However, it could yield interesting data and it is very interesting that Novartis, the leader in CAR-T cell cancer, is collaborating. Novartis also has a licence to use Celyad's patent on allogeneic T-cell production. It is therefore well placed to develop a Treg programme. TxCell holds key patents in Treg CAR technology.

Caladrius has a polyclonal Treg concept but only in Type 1 Diabetes so far. ILTOO is developing low-dose IL-2. This aims to stimulate Tregs but not other immune cells. This is the area that Celgene (via Delinia) is targeting but that project is still preclinical. ILTOO appears to be behind schedule on recruitment. In other cell types, Mesoblast is perhaps the most advanced with an NCI-run allogeneic 60 patient Phase III for GvHD intravenous. Data is may be released in H2 2017. Mesoblast has also reported promising Phase II safety and efficacy data in biologic refractory RA patients using a single dose of 1m/kg or 2 m/kg cells.

Transplantation

TxCell sees the solid organ transplant indication as a good starting indication for its CAR Treg programme. Unless a transplanted organ or tissue is a close match for the HLA type of the host, there is always a risk of rejection where the host immune system attacks the transplant. Mismatch means the number of HLA types that are the same between the donor and recipient. As the HLA system is very polymorphic with six genes to match, it is hard to get exact matches. Over four mismatches seems to be a risk factor.

The concept is that if a CAR Treg targets and binds to a non-self HLA in the graft, it will be activated locally and suppress direct cytotoxic T-cell and indirect helper T-cell antibody-led responses against the transplanted organ. Any activated CAR Treg should suppress any local immune response.

The evidence that CAR Tregs can control rejection comes from a paper by Professor Levings of the University of British Columbia with preclinical work on a mouse antibody fragment CAR Treg published (MacDonald 2016). TxCell has a collaboration with this group to target solid organ transplantation. The September 2017 preclinical data on humanised CAR Tregs is not yet

published. The project is based on the HLA-A2 CAR Treg discussed above. This will work in about 25% of cases.[1] TxCell may need to develop other HLA-type CAR Treg constructs.

Possible transplant markets

The market value for Tregs in transplant management is hard to assess. This is a niche opportunity but potentially of high value as long-term management of grafts is not optimal and as these are very expensive procedures. Graft failure is expensive to manage and often fatal so there are good reasons to use effective Treg therapies even at the Kymriah US$475,000 price point. The lung procedure should easily transfer into kidney transplant if efficacy is seen. Tregs may be useful for other organs like liver as well (c 6,000 USS transplant a year) but these are not assessed.

In the United States in 2016, there were 2,327 lung transplants, data. Over 80% of lung transplants had four or more HLA mismatches so have higher rejection risk. Survival of lung transplant patients is not good at about 50% after five years. A 2014 report indicates 1,809 lung transplants in Europe. Initial lung transplant data is planned to be available in 2020 or 2021. This may be enough for a named patient approval but a larger study will probably be needed especially for an FDA approval so 2024 is used tentatively as the expected date.

In the United States in 2016, there were 13,431 deceased donor kidney transplants. About 75% of decreased kidney donor grafts had 4 four or more mismatches. These are better managed but as a larger market offer more commercial upside and still have high medical need if a graft starts to fail due to rejection. The European markets are more fragmented. A 2014 report showed 9,912 decreased donor transplants.

An initial value assessment is shown in Exhibit 4. This is tentative but reflects known parameters. It is based on lung and kidney grafts. The patient column is the number of transplants (lung) or decrease donor grafts (kidney) each year. Accessible patients are 25% of this due to HLA type. A further adjustment is made based on the level of four or more mismatches discussed above. We estimate a relatively high market share based on medical need although lower in the EU due to funding limits. The price used is US$475,000. NPV are calculated from 2024 for 12 years biological exclusivity in the US and 10 in the EU based on an assumed 25% post-tax net margin. An alternative scenario would be a partnering deal. If so, earlier upfront payments with a lower cash flow based on royalties would be assumed instead. It seems possible that TxCell, with funding, could develop the small and specialist centre based transplant niche. We assume 12.5% probability for lung although this is high for preclinical. However, cell therapies have been approved by the FDA on fast track with limited data compared to mainstream drugs. As Kidney is less well defined, it is given a 7.5% probability.

Exhibit 4: Possible transplant markets

	Patients	Accessible	Share	Treated	Peak value (€m)	NPV	Probability	Indicative value
Lung transplant								
US	2,327	465	80%	372	€150	€93.2	12.5%	€11.7
EU	1,809	362	60%	217	€88	€51.9	12.5%	€6.5
Kidney transplant								€18.1
US	13,431	2,518	50%	1,259	€508	€315	7.5%	€23.7
EU	9,912	1,982	30%	595	€240	€142	7.5%	€10.7
								€34.3
Total	**27,479**	**5,327**	**46%**	**2,443**	**986**	**603**		**€52.47**

Source: Edison Investment Research

[1] This is because half the population is HLA-A2 positive anyway so administered Tregs will not specifically target the graft. Of the half that does not carry HLA-A2, half will get a HLA-A2 negative graft on average. This leaves 25% who are HLA-A2 negative hosts with a HLA-A2 positive graft.

These calculations indicate a value of about €71m before clinical trial costs. The overall market peak sales could be nearly €1bn. Adding in other HLA types will extend use rates and add value but as these are separate development projects, they are not included in our current forecasts.

Multiple sclerosis

The global multiple sclerosis (MS) market has grown to an estimated US$21.1bn. About $11bn of products come off-patent before 2020. Dimethyl fumarate (Tecfidera, Biogen), the leading product comes off patent in 2023. None of these drugs enable gain of function.

For a CAR Treg therapy against MS, a suitable antigen target is needed. A paper from Uppsala University Fransson (2012) showed that in a model of multiple sclerosis, Tregs diminished symptoms and enabled some nerve function to be regained. TxCell and the Center for Research in Transplantation and Immunology, will collaborate to develop CAR CD8+ Treg cells.[2] The collaboration specifically focuses on multiple sclerosis and manufacturing development. This collaboration expands TxCell's internal research in MS which is focused on CD4+ CAR Treg cells.

The prevalence of multiple sclerosis is high at about 90/100,000 people. This indicates about 650,000 cases across North America and the leading European states. The prevalence is very variable across regions and ethnic groups. It is likely that significant large trials will be required to gain approval and prove efficacy and safety so any launch before 2026 seems implausible and partnering looks essential given the clinical complexities and costs.

MS is a major possible indication and could have a high NPV estimate once more information is available. It is currently given a €10m nominal valuation. This is unchanged.

Bullous pemphigoid – interesting orphan disease

A collaboration with the Lübeck Institute of Experimental Dermatology will develop CAR Treg approaches in bullous pemphigoid (BP). The incidence of BP is poorly known. A 2008 study, Langham et al (2008), indicates perhaps 12-15,000 European cases and perhaps 12,000 US cases. The disease is treated with steroids (UK guidelines). This indication would be a niche orphan product. The market is likely to be very price sensitive and limited to very severe chronic refractory disease. It is given an unchanged nominal value of €5m.

Lupus nephritis

TxCell has a collaboration with the San Raffaele Scientific Institute in Milan to develop a CAR Treg product for lupus nephritis. Lupus nephritis is a complication of lupus where the kidney is damaged and this can lead to end stage renal failure. Currently, TxCell has not disclosed the antigen.

In the US, the Centers for Disease Control and Prevention (CDC) published two studies in 2014 (Sommers (2014), Lim (2014)). There may be about 160,000 lupus prevalence cases in the US. In Europe, accessible European markets may have a prevalence of about 170,000. This is discussed in the cited February 2017 Edison note. The epidemiology of lupus nephritis as a severe subset of lupus is complicated, but a US estimate is of about 30,000 lupus nephritis cases. The European figure will be lower because of different ethnic profile, perhaps about 17,000 cases. As it is a prevalence market, only a small proportion will be treated each year.

We have retained the €7.5m nominal value.

[2] The CTRI is a centre of excellence in the field of transplantation and immunology and affiliated to both Inserm and Nantes University

Funding and equity

The February 2017 funding raised €11.01m gross and issued 5,549,300 shares plus tradable warrants at €2 each. The warrants convert at a ratio of four warrants for three shares with each new share priced at €2.60. Of the 2016 Yorkville Advisors Global (YAG) deal using convertible loan tranches, the 27 Sept 2017 situation was as follows.

- Of the 30 loan tranches issued in August 2016 for €3m, all were converted by 8 August 2017. There are 0.35m long-dated warrants for €1.5m cash at an exercise price of €4.50.
- Of the 20 loan tranches for €2m issued on 3 November 2016, Yorkville exercised half between 8 August and 27 September for 0.74m shares. There are 10 tranches left to convert and 0.34m long-dated warrants outstanding at €2.97 that would yield €1m.

Exhibit 5 shows the origin of the 21.05m shares in issue as of 27 Sept. 2017. The 5.5m rights warrants if fully exercised by February 2018, yield €10.8m cash for 4,125 new shares. However, they are currently out of the money. Conversion of the remaining Yorkville loans is assumed.

Exhibit 5: Equity position and potential end 2018 dilution

	Shares (m)
Shares in issue 02/08/2016	13.00
Conversion of Tranche 1 bonds (inc commission)	1.63
Conversion of Tranche 2 bonds (inc commission)	0.78
Feb 2017 rights issue	5.55
Other share issues	0.09
Shares in issue 27 Sept 2017	21.05
Potential shares from rights issue warrants	4.16
Potential shares from issued loan warrants	0.69
Fully diluted (ex management options)	26.48

Source: Edison Investment Research compiled from TxCell reports. Note: Based on share price of €1.85/share

If the February 2017 rights warrants are exercised, or other funding obtained, further Yorkville drawdown can be avoided. There are €15m of possible convertible loans available from 2018.

Sensitivities: CAR Tregs create major opportunities

The CAR Treg opportunity is developing well with four clear indications. As a technology platform CAR Treg (ENTrIA) has a high deal potential. A clinical proof-of-concept study in transplant to start in late 2018 with data by H120 will be the first CAR Treg study and a milestone in the development of the technology TxCell has a granted European blocking patent until 2028; this is still under examination in the US. TxCell may need other CAR technology IP licences. The acquisition of preclinical-stage Delinia by Celgene for $300m upfront indicates that the Treg area is viewed as ripe for development, even with preclinical data. Novartis has shown some interest in Tregs. Finally, the sources of 2018 cash are still not clear with €10m needed. We have assumed that the existing rights warrants are exercised.

Valuation: Indicative value adjusted, dilution uncertain

TxCell is in a period of strategic transition. A revised valuation has been made Exhibit 6. This increases the value to €84m from €74m and rebalances the pipeline value estimates.

The following changes have been made.

- Although the manufacturing target has been met, Ovasave is on hold and TxCell is moving towards an integrated Treg technology platform. As cash flows are now uncertain, a nominal value of €20m is assigned, formerly a calculated €84m. No deal values are now assumed.

- Treg transplant indications are given a total value of €52.4m as discussed above, formerly a nominal €15m. This reflects progress on the project, Edison's assumption of a kidney transplant indication and development of a humanised CAR Treg.
- The nominal values for other CAR Treg indications have been retained.
- The assumed CAR Treg deal NPV rises to €35m, formerly €29m. This is based on a €25m deal by 2020 and a possible €300m deal on one or more specific projects in 2025. The 2025 value can be compared to the recent acquisition by Celgene of Delinia for $300m based on a preclinical Treg project (see below). A 25% deal probability is applied (formerly 20%) as CAR humanisation and improved manufacturing makes a deal more likely in our view.
- As there are now no long-term specific revenues forecast from Ovasave, costs are only projected to 2021 with net revenues used thereafter at 25% post tax on Transplant indications and 12.5% on other indications. Treg clinical trial cost estimates to 2021 are pushed back slightly but the same overall. Tax credits reduce in line with lower R&D. This takes costs to €54m before tax credits of €14m, net €40m, formerly €56m.
- Tax charges (formerly €14m) are now included in the net NPV values.
- Debt includes payments to Trizell to reacquire Ovasave of €2m, in late 2017 and €2m in late 2018. TxCell also has an innovation loan for €1.67m repaid at €0.34m per year from 2018.

Exhibit 6: Revised TxCell valuation

Item	Basis / probability	Sub category €m	Total €m
Ovasave	Nominal		20
CAR Treg transplant, lung	12.5%	18.1	
CAR Treg transplant, kidney	7.5%	31.3	
CAR Treg Multiple sclerosis	Nominal	10.0	
CAR Treg Bullous pemphigoid	Nominal	5.0	
CAR Treg Lupus Nephritis	Nominal	7.5	
Value of indications			75.0
CAR Treg potential partnering	25%		35.5
Overall value of indications			130.5
R&D (ex trial costs)		-32.4	
CAR Treg trials to 2021		-12.6	
General and administrative		-9.5	
Costs less tax credits to 2021			-54.5
Tax credits			14
Debt NPV (@1.5%)			-5.5
Pre-funding and dilution value			84.5

Source: Edison Investment Research (amounts rounded to 1 decimal place)

The value per share on the new shares in issue and fully diluted basis is in Exhibit 7. The indicative core value before conversion of all loans and issued warrants is €4.01/share. We assume conversion of all outstanding loan notes at a 15% discount to a share price of €1.75 and exercise of the rights issue warrants. This implies a value of about €3 per share. The previous diluted value was €2.83/share.

Exhibit 7: Indicative value per share

	Shares (m)	Cum total (m)	Value/share (€)
Current	21.05	21.05	4.01
Warrants and loan conversions	5.46	26.51	3.18
Management options	1.89	28.40	2.97

Source: Edison Investment Research

Financials

At year-end 2016, TxCell had €3.5m cash. The H1 report shows that the Q1 rights issue raised €11.01m gross, €10.06m net. The Yorkville convertible loans in 2016 raised €5m gross, €4.9m net,

The unconverted loans were €3.57m in December 2016 and €2.27m on 30 June 2017. The amount unconverted as of 27 September 2017 was €1m. The conversion and sale of €2.7m of shares over the first 9 months of 2017 may account for the weak share price performance. Edison expects the remaining Yorkville convertible loans to be converted and sold before December 2017.

TxCell has some complex accounting on its tax credits. Normally, these are paid in the following financial year. To bring forward the tax credit TxCell has sold the 2016 credits to Predirect Innovation 2020. Of the tax credit in 2016 of €2.8m, noted in other income, €1.6m was gained in 2016 (after presumed fees and costs of €0.3m). The remaining €0.9m was listed as "Other receivables (Note 7, DDR). The amount was realised as €0.8m net cash in H1 2017. The H1 2017 tax credit of €1.03m, is recognised as an asset. Some €0.57m is noted in the cash flow as being a pre-financed tax credit. Edison has assumed that the whole 2017 tax credit is pre-sold with €1m in other receivables at the year-end.

In H1, costs dropped. R&D costs were €3.89m (vs €5.62m) as no clinical trials were run in the period. R&D costs are expected to rise in 2018, Edison estimates by €3m, as the transplant CAR Treg trial starts. Administration and other costs fell in 2016 to €1.84m (vs €2.51m) as the Besançon internal production facility for Ovasave closed. TxCell retains manufacturing pilot facilities.

The 2017 cash outflow, as guided by management, will be about €13m. Year-end 2017 cash could be about €2m depending on cash inflows and working capital. We have assumed that the rights issue warrants convert to yield €10.8m. This is possible as conversion and sale of shares by Yorkville ceases and if further good preclinical data is announced in Q4 2017. The 2018 cash outflow indicated by Edison's forecast is c €13m; management guidance is that if the rights issue warrants are fully exercised, the cash is sufficient till the start of the transplant CAR Treg clinical study by late 2018. If the warrants remain out of the money, other financing routes will be needed. TxCell does have further €15m of Yorkville funding available. Financial estimates are in Exhibit 8.

Exhibit 8: Financial summary

€000s	2015	2016	2017e	2018e
Year end December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	920	153	262	250
Tax refund	3,718	2,794	2,340	3,240
Cost of Sales	0	0	0	0
Gross Profit	4,638	2,947	2,602	3,490
EBITDA	(10,797)	(11,947)	(8,911)	(11,110)
Operating Profit (before amort. and except.)	(9,662)	(12,047)	(9,011)	(11,210)
Intangible Amortisation	0	0	0	0
Exceptionals	(1,167)	(87)	0	0
Share based payments	(483)	(649)	(587)	(600)
Operating Profit	(11,312)	(12,784)	(9,598)	(11,810)
Net Interest	42	(18)	2	2
Profit Before Tax (norm)	(10,782)	(12,734)	(9,143)	(11,432)
Profit Before Tax (FRS 3)	(11,297)	(13,570)	(9,830)	(12,132)
Tax	0	0	0	0
Profit After Tax (norm)	(10,782)	(12,734)	(9,143)	(11,432)
Profit After Tax (FRS 3)	(11,297)	(13,570)	(9,830)	(12,132)
Average Number of Shares Outstanding (m)	12.2	13.1	21.3	25.8
EPS - normalised (c)	(88.4)	(97.5)	(42.8)	(44.3)
EPS - (IFRS) (c)	(92.6)	(103.9)	(46.1)	(47.0)
Dividend per share (c)	0.0	0.0	0.0	0.0
Gross Margin (%)	NA	NA	NA	NA
EBITDA Margin (%)	NA	NA	NA	NA
Operating Margin (before GW and except.) (%)	NA	NA	NA	NA
BALANCE SHEET				
Fixed Assets	6,938	7,032	7,004	6,954
Intangible Assets	5,907	5,911	5,933	5,933
Tangible Assets	876	799	749	699
Other	155	322	322	322
Current Assets	13,782	5,763	3,564	1,709
Stocks	0	0	0	0
Debtors	1,551	1,381	504	505
Cash	9,208	3,482	2,060	204
Other	3,023	900	1,000	1,000
Current Liabilities	(7,467)	(7,893)	(4,272)	(3,160)
Creditors	(7,467)	(7,724)	(3,934)	(2,822)
Short term borrowings	0	(169)	(338)	(338)
Long Term Liabilities	(1,664)	(3,710)	(1,536)	(1,536)
Long term borrowings	(1,641)	(3,650)	(1,324)	(1,324)
Other long term liabilities	(23)	(60)	(212)	(212)
Net Assets	11,589	1,192	4,760	3,967
CASH FLOW				
Operating Cash Flow	(10,108)	(10,417)	(12,942)	(12,579)
Net Interest	42	(18)	2	2
Tax	0	0	0	0
Capex	(214)	(337)	(100)	(100)
Acquisitions/disposals	(5,879)	0	0	0
Equity financing	7,631	270	11,618	10,821
Other	3,818	4,776	0	0
Net Cash Flow	(4,710)	(5,726)	(1,422)	(1,856)
Opening net debt/(cash)	(12,290)	(7,567)	337	(398)
HP finance leases initiated	0	0	0	1
Other	(13)	(2,178)	2,157	0
Closing net debt/(cash)	(7,567)	337	(398)	1,457

Source: TxCell accounts, Edison Investment Research

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