EDISON

Telix Pharmaceuticals

Development update

Novartis/Endocyte deal illustrates upside potential

Pharma & biotech

Novartis's US$2.1bn acquisition of Endocyte highlights the considerable potential upside that exists for Telix, if it can successfully develop its pipeline of molecularly targeted radiation (MTR) therapeutic and imaging products. It continues to make rapid progress across the portfolio, with the Atlab acquisition completed, Cardinal Health appointed as a sales and distribution agent for illumet (TLX591-CDx) in the US, a Phase I/II study of TLX101 in brain cancer initiated and the confirmatory Phase III study of TLX-250-CDx for imaging kidney tumours about to commence. Our valuation is unchanged at A$303m; value per share increases to A$1.43.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/17	0.4	(6.4)	(5.0)	0.0	N/A	N/A
12/18e	5.0	(12.7)	(6.2)	0.0	N/A	N/A
12/19e	8.4	(17.7)	(8.3)	0.0	N/A	N/A
12/20e	6.7	(15.7)	(7.4)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding exceptional items.

Novartis/Incyte deal highlights potential value

Novartis agreed earlier this month to acquire Endocyte for ~US$2.1bn. Endocyte is developing PSMA-617, a small molecule MTR therapeutic that, like Telix's TLX591, targets PSMA in prostate cancer tumours. Endocyte started a 750-patient Phase III trial of PSMA-617 in prostate cancer patients earlier this year. The US$2.1bn price that Novartis has offered for Endocyte suggests that a successful TLX591 Phase II study would add significant value to Telix.

Atlab brings TLX591 combo opportunity

In September, Telix acquired Atlab Pharma, as expected, to strengthen its IP position and gain access to clinical data and know-how related to TLX591, including certain combination therapy rights in prostate cancer. The total consideration of ~US$10m was in line with expectations, but part of the consideration was diverted to BZL Biologics, the holder of some of the underlying IP.

Impressive progress across the portfolio

Telix continues to make impressive progress developing its portfolio of MTR products. Commercialisation of illumet (TLX591-CDx) as an investigational product for imaging prostate tumours is underway in the US, with Cardinal Health appointed as a sales and distribution agent and scale-up manufacture of the kit in the US initiated. The IPAX-1 Phase I/II trial of TLX101 in brain cancer commenced recruiting patients in October. The ZIRCON Phase III study has received regulatory and ethics approval to commence recruitment at the first trial site in Australia, with the first sites in Europe expected to come on line before the end of the year.

Valuation: A$303m, A$1.43 per share

Our valuation is unchanged at A$303m.The value per share increases to A$1.43/share (from A$1.39/share), as fewer shares were issued to acquire Atlab than we had assumed (14.9m vs 20.5m). Telix is well-funded with A$37m cash.

31 October 2018

Price	**A$0.87**
Market cap	**A$185m**
	US$0.76/A$
Net cash (A$m) at 30 September 2018	37.3
Shares in issue	212.3m
Free float	58%
Code	TLX
Primary exchange	ASX
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	1.8	32.1	N/A
Rel (local)	8.9	42.8	N/A
52-week high/low		A$1.0	A$0.5

Business description

Telix Pharmaceuticals is a Melbourne-headquartered global biopharmaceutical company focused on the development of diagnostic and therapeutic products based on targeted radiopharmaceuticals or molecularly targeted radiation.

Next events

Commence recruiting ZIRCON Phase III study	Q418
Final results ZIR-dose study	Q418
Initiate TLX591 Phase III trial	Mid-2019

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Edison profile page

Novartis's US$2.1bn acquisition of Endocyte illustrates the potential value of MTR therapeutics

On 18 October, Novartis announced that it had entered an agreement to acquire Endocyte for ~US$2.1bn. Endocyte is developing ^{177}Lu-PSMA-617, a small molecule MTR therapeutic that, like Telix's TLX617, targets prostate specific membrane antigen (PSMA) in prostate cancer tumours.

Endocyte started a 750-patient Phase III trial of PSMA-617 in prostate cancer patients earlier this year. It presented encouraging data from a Phase II study of PSMA617 in prostate cancer at ASCO in June. In the 50-patient Phase II trial, 62% of subjects treated with ^{177}Lu-PSMA-617 experienced a prostate-specific antigen (PSA) decline of at least 50%. The treatment was well tolerated, with the most common side-effect being grade 1–2 dry mouth reported by 68% of subjects (66% grade 1, 2% grade 2). The occurrence of grade 3–4 hematologic toxicity was low; there were no cases of grade 4 neutropenia and only 6% of subjects experienced grade 3 neutropenia.

The US$2.1bn price that Novartis has offered for Endocyte suggests that if TLX591 can demonstrate comparable efficacy and tolerability in the upcoming Phase II study, then we would be likely to see a substantial lift in market capitalisation.

The Endocyte transaction is Novartis's second substantial acquisition of an MTR radiotherapeutic company in 12 months. In October 2017, Novartis announced an offer to acquire Advanced Accelerator Applications (AAA), for US$3.9bn. The bid was made soon after AAA received EU approval for MTR therapeutic product known as ^{177}Lu dotatate, or Lutathera, for the treatment of gastroenteropancreatic neuroendocrine tumours, a rare form of cancer. Lutathera was subsequently approved by the US FDA in January 2018. Lutathera reduced the risk of disease progression or death in NET patients by 79% in pivotal studies.

In another example of big pharma interest in the field, in February 2014 Bayer acquired Algeta for NOK16.2bn (~US$2.6bn). Algeta had developed Xofigo, a therapeutic radiopharmaceutical for patients whose prostate cancer had metastasised to their bones, which had been approved in the US and Europe in 2013.

TLX591: Atlab acquisition completed

In September, Telix completed the anticipated acquisition of Atlab Pharma to strengthen its IP position and gain access to clinical data and know-how related to its TLX591 prostate cancer therapeutic. Telix held an option to acquire Atlab for US$10m, as disclosed in the IPO prospectus.

As part of the acquisition, Telix renegotiated Atlab's background intellectual property licences with BZL Biologics, which holds a portfolio of patents originating from Professor Neil Bander's lab at Weill Cornell Medical Centre.

While the total consideration was approximately US$10m, as expected, the consideration to Atlab shareholders was reduced to US$9m in Telix shares at A$0.89 per share, and part of the consideration (US$0.5m of Telix shares and US$0.5m of warrants) was diverted to BZL biologics as partial consideration for a significant reduction in royalty rates for the background IP.

Atlab had previously conducted a number of clinical trials of a single cycle of treatment with ^{177}Lu-J591, in conjunction with Weill Cornell. Telix's TLX591 is based on an enhanced version of the huJ591 mAb.

The transaction gives Telix access to IP rights that support potential indication expansion of TLX591, including the combination use of anti-PSMA therapeutics with anti-androgen drugs such as

Zytiga and Xtandi. It also gains an extensive clinical data set in ~200 patients that is highly informative for TLX591 development, including unpublished data around dose optimisation schemes for antibody-based PSMA radiopharmaceuticals.

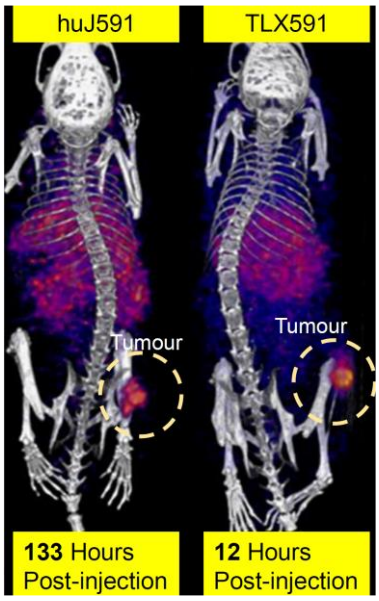
Telix has modified TLX591 to reduce bone marrow impact

Atlab conducted a number of clinical trials of ^{177}Lu-J591 in prostate cancer patients. While there was evidence of efficacy, with up to 22% of subjects experiencing a 50% reduction in PSA levels, there were also signs of bone marrow toxicity, with 74% of subjects treated having grade 3/4 haematological toxicity.

Haematological toxicity is a common feature of antibody-based therapeutic radiopharmaceuticals, which is attributed to their long plasma half-life.

Telix has engineered TLX591 to reduce the plasma half-life to 12 hours vs 133 hours for huJ591, while achieving similar levels of radiation to the tumour in animal models, as shown in Exhibit 1. Telix expects the shorter plasma half-life to reduce the haematological toxicity while maintaining anti-tumour efficacy. It also expects the antibody-based TLX591 to be less likely to damage the salivary glands and cause dry eye than small-molecule MTR products like PSMA-617.

Exhibit 1: Shorter half-life TLX591 delivers similar levels of radiation to the tumour



Source: Telix Pharmaceuticals

TLX591 development to investigate ADT combination therapy

Manufacture of drug material for TLX591 toxicology and human biodistribution studies is expected to be completed by the end of 2018. The company is on track to initiate an Australia/US multi-centre Phase II study in mid-2019.

The Phase II trial is expected to focus on combining TLX591 with androgen deprivation therapy (ADT) in relatively early-stage patients. ADT with the blockbuster drugs Xtandi (enzalutamide) and Zytiga (abiraterone) blocks production of testosterone and inhibits prostate cancer tumour growth, and is standard of care for medium- and high-risk prostate cancers after prostatectomy, and for treating recurrent and metastatic disease.

TLX591 binds to PSMA, which is expressed in very high levels in the prostate but in low levels on most other normal cells. PSMA is significantly over-expressed in prostate cancer cells and some other solid tumours.[1]

Treatment with ADT drugs increases the expression of PSMA on prostate cancer tumours, making them better targets for TLX591. Telix plans to investigate combining TLX591 with a relatively short course of ADT hormone therapy. If this combination is effective at controlling tumour growth or recurrence, it could potentially allow a 'treatment holiday' from ADT therapy and its negative effects on sexual function, mood, energy levels and cognitive function.

Successful development of TLX591 as a combination therapy would allow its use at an earlier stage of the disease and consequently provide a larger market opportunity than our current scenario of use in late-stage disease. We currently model the addressable market being 90% of prostate cancer deaths, which is equivalent to 16% of new prostate cancer patients each year in the US. If use is extended to earlier-stage patients, we estimate that the addressable market could almost double to ~30% of new cases, which would boost estimated peak sales for TLX591 from US$1.1bn to US$2.0bn. We will review our assumptions for the addressable market for TLX591 when we see the results of clinical studies of the combination therapy.

Commercial supply of illumet (TLX591-CDx) underway

Telix recently launched commercial supply of the illumet investigational prostate cancer imaging agent in the US. Illumet, previously known as TLX591-CDx, is a 'cold kit' for the preparation of radiolabelled ^{68}Ga-PSMA-11 for imaging prostate cancer with Positron Emission Tomography (PET). The illumet product was developed by ANMI SA of Belgium, and is being commercialised by Telix in the US under a joint venture agreement.

Telix took an important step forward in early October when it entered into a sales and distribution agreement for the illumet kit with Cardinal Health. Cardinal Health operates the largest radiopharmaceutical network in the US, and prepares more than 20 million unit doses of radiopharmaceuticals annually.

Cardinal Health can use the kit to compound doses of ^{68}Ga-PSMA as well as distributing the kit directly to qualified customers.

While illumet has not yet obtained FDA approval, it can be sold as an investigational product for use in qualified investigator-sponsored clinical trials. Telix has submitted a Drug Master File (DMF) providing confidential detailed information about the manufacture of illumet to the FDA, which has reviewed and accepted the documentation.

Two active INDs are already in place that reference the DMF and enable illumet to be used in clinical studies. The Memorial Sloan Kettering Cancer Center has launched an expanded-access study (NCT03204123), which allows the kit to be used to image 500 prostate cancer patients at its clinics. Endocyte is using illumet kits for screening patients in its 750-subject VISION Phase III prostate cancer trial.

Sales of the illumet kit as an investigational product will generate initial revenues for Telix and will allow clinicians to gain experience with its utility for identifying prostate cancer metastases and sites of local recurrence. First revenues from the illumet kit are expected in the current quarter.

In order to capitalise on the full commercial potential of illumet, Telix is developing a strategy that will enable it to seek full FDA approval, which would bring higher reimbursement and allow active marketing of the kit. It plans to hold a pre-NDA meeting with the FDA in Q418, where it will propose

1 Sterzing et al; Eur J Nucl Med Mol Imaging (2016) 43:34–41

a Phase III programme for illumet that is based on blinded re-reads of existing PET scan data. If this strategy is acceptable to the FDA, then management anticipates an NDA submission in 2019. Given that the FDA has already reviewed the manufacturing and QC data in the DMF, there is the potential that illumet could be approved by the FDA by the end of 2019 (we model a more conservative timeline with a potential approval in 2020). The estimated cost of a Phase III study and NDA filing based on re-reads is US$2m.

In response to considerable clinical interest in illumet, Telix has commenced scale-up manufacturing of illumet in the US; by the end of the year, it will be made at a 20,000-unit scale at an FDA-inspected facility. With the increased supply due to come on line shortly, it has taken the opportunity to expand its partnership with ANMI, so that Telix will sell US-manufactured cold kits to ANMI for distribution outside the US.

ZIRCON Phase III at the starting line

Telix is preparing to commence recruitment in the ZIRCON Phase III trial for imaging clear cell renal cell carcinoma (ccRCC) with TLX250-CDx (^{89}ZR-girentuximab), having completed the necessary preparations, including receiving regulatory and ethics approval to commence recruitment at the first of four planned sites in Australia. The first sites in Europe are expected to come on line before the end of the year.

The Phase III study is planned to recruit approximately 250 cancer patients undergoing surgery to remove suspicious kidney masses in at least 15 sites in Europe, Australia and the US. Management expects the Phase III study to complete by Q319. The study will determine the sensitivity and specificity of TLX250-CDx PET imaging to detect ccRCC in comparison with histology examination of tissue samples collected during surgery.

In recent weeks, Telix has appointed Netherlands-based Radboud Translational Medicine to manufacture TLX250-CDx for clinical trials (and eventual commercial production) in Europe. It has selected Cyclotek to manufacture and supply Australian clinical trial sites, as well as to act as a back-up production site for the global multi-centre Phase III trial.

It has reported the results of an interim analysis of the first five subjects in the 10-patient dosimetry bridging study (ZIR-dose), which confirmed that the TLX250-CDx product that contained 10mg of the girentuximab targeting antibody was superior to the 5mg product, with a 50% lower dose of radiation absorbed by the liver and a 25% lower dose in the lower intestinal dose. Eight of the target of 10 subjects have been recruited and the study is expected to complete before the end of the year.

A comparison with historical dosimetry data showed that the change of isotope from ^{124}I to ^{89}Zr has reduced the dose of radiation absorbed by the patient by approximately 25%. This suggests that in addition to improving image quality, the change in isotope may also have improved patient safety.

The interim analysis has given Telix confidence that it has identified the right dosing and dosimetry for TLX250-CDX, enabling it to proceed with dosing the first patients in the ZIRCON Phase III study.

We expect the primary application of TLX250-CDX to be to help distinguish between ccRCC (the most serious form of kidney cancer) and other renal masses as part of the initial diagnostic work-up. Kidney cancer is the eighth most common cancer, and is expected to account for 65,340 new cases and 14,970 deaths in the US in 2018.[2] Globocan predicts that in 2020 there will be 423,000 new cases and 184,000 deaths from kidney cancer worldwide.

2 https://seer.cancer.gov/statfacts/html/kidrp.html

We estimate that the addressable market for TLX250-CDX is equivalent to 50% of new kidney cancer cases each year, with half of use being for initial diagnosis and the balance being for applications such as detecting metastatic disease, screening patients for suitability for MTR therapy and monitoring response to therapy with targeted agents.

TLX101 GBM trial opens for recruitment

The IPAX-1 trial of TLX101 in patients with glioblastoma (GBM), commenced recruiting patients in Austria in mid-October, having received ethics approval from two hospitals in Austria and regulatory approval from that country's Federal Office for Safety in Health Care. Additional clinical sites in Belgium, the Netherlands, Germany, Switzerland and Australia will follow, subject to ethics and regulatory approvals. GBM is the most common and most aggressive form of brain cancer.

The Phase I/II dose-ranging study is evaluating the safety, tolerability, dosing schedule and preliminary efficacy of single or repeated injections of TLX101 in patients whose GBM has recurred following previous treatment. It is intended to recruit at least 35, and potentially up to 55, subjects in the study.

Subjects will be administered TLX101 in conjunction with external beam radiation therapy, thereby simultaneously irradiating both bulky lesions and small metastases. This protocol will capitalise on the fact that, in addition to delivering the ^{123}I radioisotope directly to GBM tumour cells, TLX101 also acts as a radio-sensitiser, increasing the sensitivity of cells to radiation.

The preliminary efficacy assessment will be based on post-treatment imaging and is expected to read out by the end of 2019.

Telix has appointed the Austrian company Siebersdorf Labor to manufacture TLX101 for global distribution for clinical trials and for compassionate use programmes.

Valuation

We have updated the cash balance to 30 September 2018 and rolled forward the DCF model, which leaves our valuation of Telix is unchanged at A$303m. It is based on a risk-adjusted discounted cash flow model, which includes our estimates of the future milestone payments and royalty streams for TLX250 and TLX591, plus profits from commercialisation of TLX250-CDx, illumet and TLX101, as listed in Exhibit 2. We have extended our cash flow forecasts out to 2037 (supported by 12 years of biologicals market exclusivity in the US and 10 years in Europe) but have not included any terminal valuation.

Our valuation per share has increased to A$1.43 per share (vs A$1.39 per share) as the number of shares issued to acquire Atlab was lower than we had assumed in our initiation report (14.9m vs 20.5m). The lower number of shares was due to the higher share value at the time of the transaction (A$0.89 vs our forecast of A$0.66) and the fact that US$0.5m of the US$10m total consideration was paid as warrants (exercisable at A$1.34) rather than shares. After dilution for options and warrants on issue, our fully diluted valuation is A$1.40per share (vs A$1.36 per share).

Exhibit 8 shows our (unchanged) market assumptions for TLX250, TLX250-CDx, TLX591, illumet and TLX101 imaging and therapeutic products, and the rNPV for each product. We have offset the risk-adjusted trial cost against revenue for each indication.

Exhibit 2: Telix sum-of-the-parts DCF

	Base case likelihood (%)	rNPV (A$m)	rNPV/sh (A$)	Assumptions
TLX250-CDx kidney cancer imaging	75%	47.8	$0.23	Global peak sales of US$70m. For the US, assumes 65,300 kidney cancer cases/year, 50% candidates for imaging, 25% penetration; for the EU assumes 93,000 cases/year, 50% candidates for imaging, 20% penetration; pricing US$3,500 per patient, 30% discount in Europe; launch 2021; assume profit margin after deducting royalty to Wilex equal to 30% of net sales. R&D cost: A$12m to compete Phase III.
TLX250 kidney cancer therapeutic	20%	49.3	$0.23	Global peak sales of US$470m. For the US assumes 65,300 kidney cancer cases/year, 20% eligible for treatment, 20% penetration; for the EU assumes 93,000 cases/year, 20% eligible, 16% penetration; pricing US$70k per patient, 30% discount in Europe; launch 2024 – biologicals market exclusivity to 2036 in US, 2034 in Europe; assume receives 12% net royalty. R&D cost: A$4m for two small company funded Phase II studies, then out-license.
illumet prostate cancer imaging	80%	55.9	$0.26	US peak sales of US$80m assuming 165,000 new cases/year, 75% candidates for imaging; 15% penetration; revenue to the Kyzeo JV US$3,500 per test; commercial launch as investigational test 2018, FDA approval 2020; assume Telix profit share equal to 20% of JV net sales. R&D cost: US$2m for a Phase III study based on re-read of existing scans.
TLX591 prostate cancer therapeutic	20%	102.6	$0.48	Global peak sales of US$1,080m. For the US assumes 29,400 deaths/year, 90% eligible for treatment, 15% penetration; for the EU assumes 84,000 deaths/year, 90% eligible 12% penetration; pricing US$70k per patient, 30% discount in Europe; launch 2025 – biologicals market exclusivity to 2037 in US, 2035 in Europe; assume receives 12% net royalty. R&D cost: A$20m for Phase II, then out-license.
TLX101 brain cancer therapeutic	10%	36.1	$0.17	Global peak sales of US$530m assuming annual US incidence of GBM of 11,000 cases, 90% eligible for therapy, 25% penetration; EU GBM incidence 21,500, 90% eligible, 15% penetration; pricing US$70k per patient, 30% discount in Europe; launch 2025; 15% royalty on net sales. R&D cost: A$6m for Phase I/II, A$25m for Phase III.
SG&A to 2024		-25.5	-$0.12	
Portfolio total		**266.1**	**$1.25**	
Cash (30 September 2018)		37.3	$0.18	
Enterprise total		**303.4**	**$1.43**	

Source: Edison Investment Research. Note: NPV adjusted for tax at an effective tax rate of 25%. We assume that the addressable markets grow at 3% per year. We show our estimate of net royalty rate or profit margin after deducting estimated trailing royalties to IP holders.

Exhibit 3: Financial summary

A$000s	2017	2018e	2019e	2020e
Year end 31 December	AASB	AASB	AASB	AASB
PROFIT & LOSS				
Sales, royalties, milestones	0	0	176	726
Other (includes R&D tax rebate)	403	5,000	8,206	6,012
Revenue	403	5,000	8,382	6,738
R&D expenses	(2,977)	(12,000)	(20,000)	(16,000)
SG&A expenses	(3,538)	(6,049)	(6,229)	(6,419)
Other	(291)	0	0	0
EBITDA	(6,403)	(13,049)	(17,847)	(15,681)
Operating Profit (before GW and except.)	(6,403)	(13,049)	(17,868)	(15,718)
Intangible Amortisation	(4)	(151)	(136)	(122)
Exceptionals	0	0	0	0
Operating Profit	(6,407)	(13,200)	(18,004)	(15,840)
Net Interest	30	488	317	98
Profit Before Tax (norm)	(6,377)	(12,712)	(17,687)	(15,742)
Profit Before Tax (reported)	(6,377)	(12,712)	(17,687)	(15,742)
Tax benefit	0	0	0	0
Profit After Tax (norm)	(6,377)	(12,712)	(17,687)	(15,742)
Profit After Tax (reported)	(6,377)	(12,712)	(17,687)	(15,742)
Average Number of Shares Outstanding (m)	128.0	204.9	212.3	212.3
EPS - normalised (c)	(4.98)	(6.21)	(8.33)	(7.42)
EPS - diluted	(4.98)	(6.21)	(8.33)	(7.42)
Dividend per share (A$)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	1,549	9,295	9,238	9,179
Intangible Assets	1,508	1,357	1,222	1,099
Tangible Assets	5	105	184	247
Investments	35	7,832	7,832	7,832
Current Assets	49,545	36,883	18,139	6,483
Stocks	0	0	0	0
Debtors	339	4,735	7,935	5,735
Cash	48,759	31,701	9,757	301
Other	447	447	447	447
Current Liabilities	(1,468)	(1,468)	(354)	(382)
Creditors	(1,123)	(1,123)	(9)	(36)
Short term borrowings	(345)	(345)	(345)	(345)
Other	0	0	0	0
Long Term Liabilities	(332)	(332)	(332)	(4,332)
Long term borrowings	0	0	0	(4,000)
Other long term liabilities	(332)	(332)	(332)	(332)
Net Assets	49,293	44,377	26,690	10,948
CASH FLOW				
Operating Cash Flow	(6,060)	(17,446)	(22,161)	(13,453)
Net Interest	29	488	317	98
Tax	0	0	0	0
Capex	(6)	(100)	(100)	(100)
Acquisitions/disposals	4	0	0	0
Equity Financing	55,561	0	0	0
Dividends	0	0	0	0
Other	0	0	0	0
Net Cash Flow	49,528	(17,058)	(21,944)	(13,456)
Opening net debt/(cash)	1,115	(48,414)	(31,355)	(9,411)
HP finance leases initiated	0	0	0	0
Other	0	0	0	0
Closing net debt/(cash)	(48,414)	(31,355)	(9,411)	4,045

Source: Edison Investment Research, Telix Pharmaceuticals accounts

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