EDISON

Prescient Therapeutics

Clinical update

PTX-100 to target RhoA-mutant lymphomas

Pharma & biotech

Prescient Therapeutics is planning a clinical trial of PTX-100 in RhoA-mutant lymphomas, a niche indication where the company could potentially conduct a pivotal study before out-licensing. It has resumed recruitment in the Phase Ib component of trials of lead anti-cancer compound PTX-200 in acute myeloid leukaemia (AML) and ovarian cancer, and is working with the FDA to recommence its Phase II breast cancer study. The company had A$6.9m cash on 30 September, sufficient to fund operations into FY19. We value Prescient at A$62m or A$0.29 per share.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/16	1.0	(1.8)	(2.1)	0.0	N/A	N/A
06/17	1.1	(2.6)	(1.2)	0.0	N/A	N/A
06/18e	0.6	(4.2)	(2.0)	0.0	N/A	N/A
06/19e	0.7	(8.4)	(4.0)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding exceptionals and share-based payments.

PTX-100 to target RhoA-mutant lymphomas

Prescient has announced that it will resume clinical development of its second anti-cancer drug, PTX-100, in rare lymphomas where mutations of RhoA are common, such as angio-immunoblastic T-cell lymphoma. PTX-100 blocks an essential step in the activation of many downstream signalling proteins in the Ras oncogene signalling pathway, including RhoA. Clinical studies in this indication are expected to commence in mid-2018, after preclinical studies to confirm the mechanism of action of PTX-100 in RhoA mutant tumours are completed. The smaller trial sizes and potential for accelerated approval in this niche indication mean that Prescient could potentially conduct a pivotal study itself before seeking to out-license.

PTX-200 AML and ovarian cancer trials recommenced

Recruitment has recommenced in Phase Ib/II trials of PTX-200 in AML and ovarian cancer, after the FDA lifted clinical holds put in place in May after a patient on the breast cancer study passed away from liver failure. The study of PTX-200 in combination with cytarabine in AML patients will be closely watched, as an earlier Phase I trial showed preliminary evidence of activity in this disease. Prescient is addressing with the FDA changes to risk management and patient protocols so that recruitment can recommence in the Phase II component of the breast cancer study. One of the eight patients evaluated so far in the Phase Ib expansion cohort of the breast cancer study experienced a pathologic complete response (pCR).

Valuation: A$62m or A$0.29 per share

We reintroduce our valuation of Prescient at A$62m or A$0.29 per share. Taking into account 9.5m potential deferred acquisition shares and 62m options, we calculate a diluted value of A$0.26 per share (this does not account for any potential dilution from an additional ~A$6m funding that we estimate may be required in FY19).

20 November 2017

Price	**A$0.07**
Market cap	**A$14m**
	US$0.76/A$
Net cash (A$m) at 30 September 2017	6.9
Shares in issue	211.3m
Free float	69%
Code	PTX
Primary exchange	ASX
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(4.4)	(17.1)	(0.9)
Rel (local)	(2.5)	(22.5)	(13.8)
52-week high/low	A$0.13	A$0.07	

Business description

Prescient Therapeutics is an ASX-listed biotechnology company focused on developing novel products for the treatment of cancer. It has two products, PTX-100 and PTX-200 in clinical development for a range of cancers. Lead candidate PTX-200 is a specific inhibitor of Akt, a key component of cancer-signalling pathways.

Next events

Completely enrol PTX-200 AML second dose escalation cohort	H217
PTX-200 breast cancer full Phase Ib data	TBA
Initiate PTX-100 haematological cancer pilot study	mid-2018

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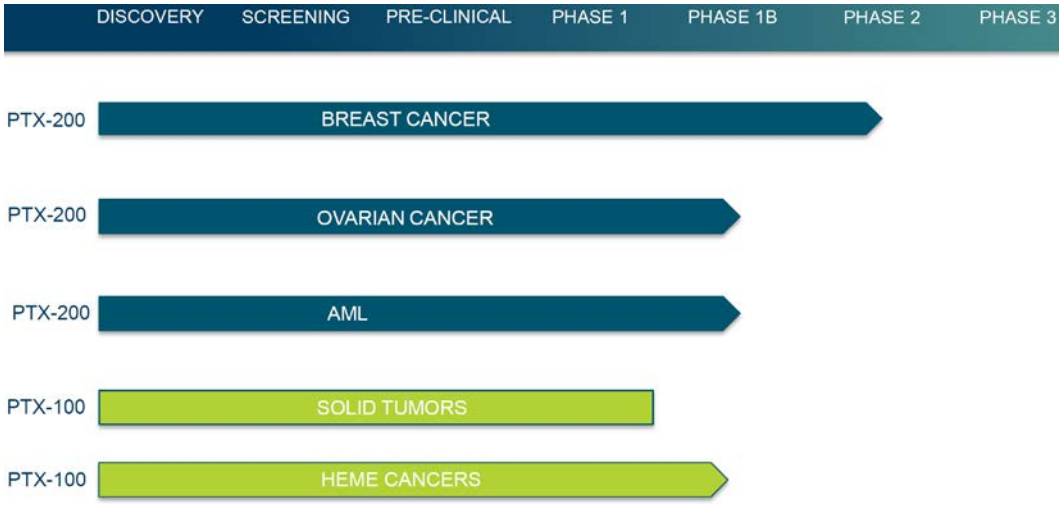
Current clinical development focused on PTX-200

Prescient has two clinical-stage anti-cancer compounds in its pipeline: PTX-200 and PTX-100.

PTX-200 is a specific inhibitor of Akt, a key component of signalling pathways known to promote cancer cell growth and resistance to chemotherapy. US-based Phase Ib/II trial programmes have commenced for the three priority PTX-200 programmes in breast and ovarian cancer and AML, as shown in Exhibit 1. Recruitment in the AML and ovarian cancer studies has recommenced following the lifting of the clinical hold on PTX-200 studies. The ovarian and breast cancer trials have been partly funded by US government grants.

The company's second pipeline drug, PTX-100, which inhibits geranylgeranyltransferase-1 and the Ras oncogene pathway, was well tolerated in a Phase I trial. Prescient recently completed a strategic review of the optimal indications for this drug, and announced on 3 October that it intends to undertake clinical studies of PTX-100 in haematological cancer, focusing on rare lymphomas.

Exhibit 1: Prescient's clinical stage product pipeline



Source: Prescient Therapeutics October 2017 investor presentation

PTX-100 to target RhoA-mutant haematological cancers

PTX-100 blocks the important cancer growth enzyme geranylgeranyltransferase-1 (GGT1), which performs an essential step in the activation of many of the downstream signalling proteins in the Ras oncogene signalling pathway, including Ral and RhoA. GGT1 attaches a geranylgeranyl (GG) lipid to the signalling proteins, which enables them to move to their proper cellular location and become fully active. A Phase I study showed that ~30% of patients with advanced solid tumours had stable disease following PTX-100 therapy.

A recent review paper highlighted that somatic mutations in the RhoA gene are common in a number of haematological cancers, including angio-immunoblastic T-cell lymphoma (53-71% of cases), peripheral T-cell lymphoma not otherwise specified (PTCL-NOS, ~17%), adult T-cell leukaemia/lymphoma (15%), Burkitt lymphoma (~8%) and diffuse large B-cell lymphoma (DLBCL, ~5%).

RhoA mutations were also common in diffuse-type gastric cancer, occurring in 14-25% of cases.

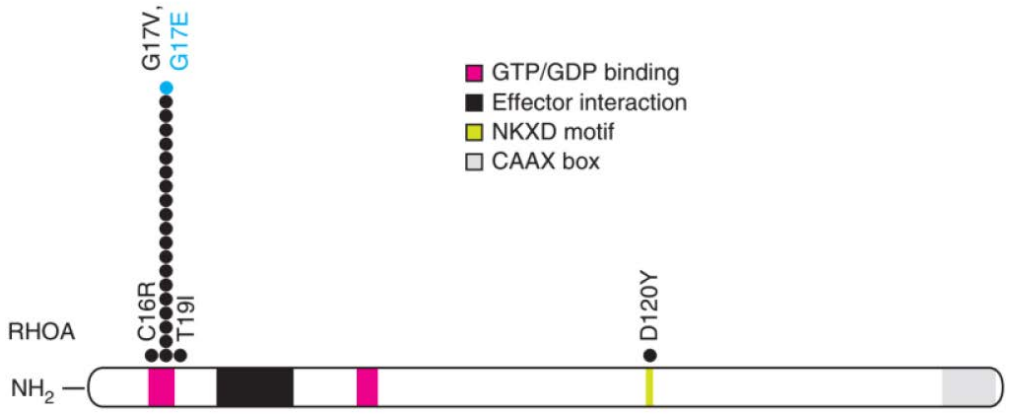
Exhibit 2 shows that in angio-immunoblastic T-cell lymphoma (AITCL) and PTCL-NOS, the two lymphomas where RhoA mutations were most common, the changes were almost exclusively G17V mutations (ie the glycine at amino acid position 17 was replaced by valine).

The G17V mutation prevents the RhoA protein from switching to its active form by binding to a molecule known as GTP. The G17V mutation acts in what is called a "dominant negative" fashion in AITCL, ie, the presence of one copy of the G17V mutation blocks RhoA signalling, despite the presence of a normal or "wild-type" RhoA gene on the other copy of the chromosome in the tumour cell. Palomero et al[1] proposed that the G17V mutation inhibits signalling from the normal or wild-type RhoA gene by binding and sequestering the active GEF (guanine exchange factor) proteins that would normally activate RhoA signalling as part of the RAS signalling cascade.

The company is undertaking a programme of preclinical studies while it prepares for a clinical trial of PTX-100 in RhoA mutant lymphomas. We expect that some of these preclinical studies would seek to determine whether treatment with PTX-100 can prevent the sequestration of active GEF proteins and restore normal or "wild-type" RhoA signalling in G17V mutant cells.

The situation is different in ATL, where G17V is less common and the most frequent mutation, C16R, results in over-activation of RhoA signalling. This suggests that both loss and gain of RhoA functions can play a role in this lymphoma. We would expect that preclinical studies would also investigate the potential role of PTX-100 as a RhoA inhibitor in mutations that result in over-activation of RhoA.

Exhibit 2: RhoA structure plus mutations reported in AITL and PTCL-NOS



Source: Prescient Therapeutics October 2017 investor presentation

The RhoA-mutant lymphomas represent niche indications with small patient populations, which offer the potential advantage of smaller trial sizes and the potential to access accelerated approval pathways after completing Phase II trials.

For example, in June 2016 the Spanish pharmaceutical company PharmaMar initiated a pivotal Phase II trial of its drug plitidepsin in AITCL. PharmaMar's single-arm study in 60 patients is intended to support an application for marketing approval in the US.

In light of the company's announcement that it intends to resume clinical development of PTX-100 in RhoA-mutant lymphomas, we now model RhoA-mutant lymphomas as the lead indication for PTX-100 in our indicative valuation, in place of the breast cancer indication that we previously modelled.

1 Palomero et al; Recurrent Rhoa Mutations In Peripheral T-Cell Lymphoma; *Blood* 2013 122:846;

FDA lifts clinical hold on two PTX-200 trials, still addressing breast cancer study

The company's three clinical studies of PTX-200 were all placed on clinical hold by the FDA in May 2017 after a patient with late-stage breast cancer who was participating in the PTX-200 study in that disease developed liver failure and passed away. The patient was also being treated with paclitaxel, which can affect liver metabolism. In his submission to the FDA, the principal investigator in the trial assessed the cause of the serious adverse event (SAE) as possibly related to paclitaxel, possibly related to PTX-200, and possibly related to the diabetes drug pioglitazone.

The FDA subsequently lifted the clinical hold on the AML study in September and on the ovarian cancer trial in November, following agreement on changes to trial protocols to improve patient safety. The changes included updated risk management plans, more frequent liver function testing, and changes to recruitment criteria so that patients with a history of liver disease are no longer eligible to participate in the studies.

Prescient is addressing with the FDA the appropriate changes to risk management and patient protocols to improve safety and allow the lifting of the clinical hold that remains in place on the trial of PTX-200 in patients with breast cancer.

AML Phase Ib trial recruiting second-dose cohort

Following the lifting of the clinical hold in September, Prescient has resumed dosing patients in the second of four dose cohorts in the Phase Ib component of the Phase Ib/II programme investigating PTX-200 in combination with cytarabine in AML (ClinicalTrials.gov: NCT02930109). AML is a cancer of the blood and bone marrow that is most common in adults over the age of 60. About two-thirds of patients respond to standard induction chemotherapy with duanorubicin and cytarabine. However, about half of patients who initially respond eventually relapse. There are limited treatment options for relapsed or refractory AML patients and the five-year survival rate is ~25%. The American Cancer Society estimates that there will be ~21,380 cases of AML and ~10,590 deaths from the disease in the US in 2017.

In a previous Phase I study, 17 of 32 AML patients achieved stable disease after one treatment cycle, and three patients achieved a >50% reduction in the number of blast (cancerous) cells in the bone marrow. One patient showed a marked reduction in circulating white-cell count and spleen size.

The Phase Ib part of the current study programme will enrol 15-18 patients with relapsed or refractory AML. Recruitment at the Moffitt Cancer Center in Florida began in December 2016 under the guidance of Professor Jeffrey Lancet, and the Yale Cancer Center in Connecticut is now also recruiting patients. The trial will test four different doses of PTX-200 in combination with the standard-of-care chemotherapy drug, cytarabine. Dosing of PTX-200 started at 25mg/m^2 and will increase by 10mg/m^2 for each subsequent dose level. Once the recommended Phase II dose is identified, approximately 25 patients will be tested in a Phase IIa cohort.

An investor conference call in April featuring Prescient CSO Professor Said Sebti and Professor Lancet highlighted that the 70-75% of AML patients who have hyper-phosphorylated/activated Akt have shorter survival and a lower response to chemotherapy, and identified inhibition of p-AKT as a strategy to broaden the proportion of AML patients who respond to chemotherapy. The previous Phase I trial showed preliminary evidence that PTX-200 is active as a single agent in a very refractory group of AML patients. The current Phase Ib trial is testing PTX-100 in combination with the standard of care chemotherapy drug, cytarabine, at an earlier stage of disease, so efficacy is expected to be considerably higher.

In the Phase IIa component, the null hypothesis is that there will be a 20% response rate to cytarabine on its own, and that a 40% response rate would be evidence of meaningful clinical activity of PTX-200. We understand that a response rate – complete remission (CR) plus CR with incomplete hematologic recovery (Cri) – of at least 33% in the Phase IIa expansion cohort would be considered to be consistent with an underlying 40% response rate, and would justify further investigation in AML patients. Professor Lancet said that one option if the response rate was slightly short of the target level would be to expand the Phase IIa trial to get a more statistically reliable estimate of the underlying response rate.

Prescient has been granted Orphan designation for PTX-200 for the treatment of AML. Benefits include seven years of guaranteed market exclusivity if regulatory approval for AML is granted.

Breast cancer study to progress to Phase II when clinical hold lifted

Prescient announced in April that its Phase Ib trial of PTX-200 in patients with Stage IIB-IV (ie locally advanced or metastatic) HER2-negative breast cancer has met its pre-specified safety and tolerability success criteria and will now progress to Phase IIa (ClinicalTrials.gov: NCT01697293).

In the first part of the Phase Ib trial, 17 patients were enrolled in several dose cohorts that determined the recommended Phase II dose (RP2D) to be 35mg/m^2 together with 80mg/m^2/week of paclitaxel. The Phase Ib trial then enrolled an expansion cohort of 12 patients who received standard doxorubicin therapy and surgery at the completion of PTX-200/paclitaxel combination therapy. Eight patients in the expansion cohort have been evaluated for clinical response, with one patient (12.5%) experiencing a pCR – complete disappearance of disease on microscopic assessment of excised tumour. Of the remaining seven patients, four had partial responses, two exhibited stable disease and one had progressive disease.

The Phase IIa component of the trial will recruit women with locally advanced breast cancer (stage IIB-IIIC disease) who will undergo the same treatment regimen as the Phase Ib expansion cohort. Five of the 12 patients enrolled in the expansion cohort had locally advanced disease and their responses will be included in the Phase IIa study analysis. Three of these five patients have gone on to surgery and one patient, with stage IIIb hormone receptor positive, HER2-negative breast cancer exhibited a pCR.

The trial is being led by Professor Joseph Sparano at the Albert Einstein College of Medicine in New York, and has been partly funded by the US National Cancer Institute. Florida's Moffitt Cancer Center joined the study in the 2016, under the direction of lead investigator Dr Heather Han.

Ovarian cancer progresses to second cohort

In December, the company also dosed the first subject in the second (25mg/m^2) dose cohort of its Phase Ib trial in patients with recurrent or persistent platinum-resistant ovarian cancer (ClinicalTrials.gov: NCT01690468). In this study, PTX-200 is being combined with the standard-of-care chemotherapy drug, cisplatin. PTX-200 has shown synergistic activity in combination with cisplatin in preclinical studies, so it is hoped that adding it to the standard cisplatin regimen will improve response rates and survival in women with ovarian cancer.

Valuation

We reintroduce our valuation of Prescient at A$62m, including A$6.9m cash on 30 September 2017; this is equivalent to A$0.29/share. The diluted valuation is A$0.26/share after accounting for 62m options and 9.5m deferred acquisition shares.

Following the delays to the PTX-200 development programme due to the clinical hold, we now assume that the programme will be out-licensed in FY20 vs FY18 previously, with launches for breast and ovarian cancer in 2024 vs 2023 previously.

We have switched to RhoA-mutant lymphoma as the lead indication for PTX-100 (replacing breast cancer). We assume that a pilot study of PTX-100 will be initiated in mid-2018, and that the drug will be partnered in FY22 following the completion of a pivotal study.

Our valuation is based on a risk-adjusted DCF model, which includes our estimates of the future milestone payments and royalty streams for the four lead programmes in Prescient's portfolio, namely PTX-200 in breast and ovarian cancers and AML, and PTX-100 in RhoA-mutant lymphoma. We have extended our cash flow forecasts out to 2032 applying a 12.5% discount rate, but have not included any terminal valuation. We assume a long-term exchange rate of US$0.76/A$.

Our model includes risk-adjusted upfront payments and clinical/regulatory milestones (but not sales milestones) from a potential licensing deal, based on average Phase II deal metrics from BioCentury. We assume that both PTX-100 and PTX-200 are sub-licensed to separate marketing partners; we assume that the licence deal for PTX-200 includes a US$20m upfront payment and US$120m in clinical and regulatory milestone payments, while for a PTX-100 deal post the completion of a pivotal study we assume A$50m upfront and US$100m regulatory milestones.

Exhibit 3 shows our market assumptions for PTX-100 and PTX-200, and the contribution of product royalties and milestone payments to the rNPV. In valuing individual products we have offset half the risk-adjusted trial costs against royalty income for each disease indication, and half against milestone revenue (previously 100% of R&D costs were offset against royalty revenue).

Exhibit 3: Prescient sum-of-the-parts DCF

	Base-case likelihood	rNPV (A$m)	rNPV/sh (A$)	Assumptions
1. Breast cancer PTX-200	15%	14.3	$0.07	Global peak sales of US$550m assuming annual US incidence of 233k, 15% of patient candidates for neoadjuvant therapy and 63% of these are HER2 negative; 25% penetration; pricing of US$50k. Global sales 2x US sales; launch 2024; assume receives 15% royalty on net sales, pays away 25% of licensing revenue to Cahaba.
2. Ovarian cancer PTX-200	15%	5.4	$0.03	Global peak sales of US$940m assuming annual US incidence of 22k, 45% penetration; price US$50k. Global sales 2x US sales; launch 2024; assume receives 15% royalty on net sales, pays away 25% of revenue to Cahaba.
3. AML PTX-200	15%	23.8	$0.11	Global peak sales of US$940m assuming annual US AML incidence of 21k, 45% penetration; pricing of US$50k. Global sales 2x US sales; launch 2025; assume receives 15% royalty on net sales, pays away 25% of licensing revenue to Cahaba.
4. RhoA-mutant lymphomas PTX-100	10%	5.9	$0.03	Global peak sales of US$290m assuming US incidence of 2.0k, 50% penetration; pricing of US$100k. Global sales 2x US sales; launch 2023; assume net royalty 18% after pay-aways to Yale.
5. PTX-200 milestones		7.1	$0.03	Assumes potential licensing upfront and milestones total US$140m (US$31m after risk adjustment); assume 15% of upfront payment and 25% of milestones paid away to Cahaba.
6. PTX-100 milestones		8.5	$0.04	Assumes potential licensing upfront and milestones total US$150m (US$21m after risk adjustment); assume milestones potentially paid away to Yale total US$5m (unrisked), US$1.1m risk adjusted.
7. SG&A to 2022		-10.2	-$0.05	
Portfolio total		55.0	$0.26	
Cash at September 2017		6.9	$0.03	
Enterprise total		61.9	$0.29	

Source: Edison Investment Research

Our base case valuation of A$62m assumes that marketing rights to PTX-100 are out-licensed in FY22 at the completion of a pivotal study. Given that RhoA-mutant lymphoma is a niche patient population, Prescient could potentially commercialise PTX-100 in the US with a small sales force. We examined a scenario where the company commercialised PTX-100 in the US and earned an operating profit margin of 45% (before pay-aways to Yale) and out-licensed ex-US rights in a deal with US$100m of upfront and milestone payments (vs US$150m in the base case). At this early stage of development self-commercialisation in the US would add a modest A$1m to our valuation, but it would be an attractive option if a pivotal study of PTX-100 in this indication is successful.

Sensitivities

Drug development risk: prospective cancer treatments have a high hurdle rate to reach approval, including lengthy and costly development programmes and high rates of failure.

Partnership/transactional risk: the timing for PTX-100 and PTX-200 development will depend on Prescient's ability to secure a development partner or acquirer at favourable terms, as we do not expect it to independently develop or fund PTX-200 at Phase III. Commercial success will also depend on the marketing capabilities of the potential partner.

Deferred acquisition consideration: a total 9.5m shares (4.5% of current issued capital) are payable if all clinical hurdles are met.

Financing risk: we estimate that the company may require A$6m of additional funding in FY19 to support its planned clinical trial programme, and this is not reflected in our diluted valuation of A$0.26/share. We estimate that a pivotal clinical trial programme for PTX-100 in RhoA-mutant lymphoma and the development of a companion diagnostic test could cost ~US$16m, including US$15m in FY21-23. Challenges in obtaining funding on desirable terms for future studies could lead to programme delays or unfavourable dilution to equity holders.

Financials

NPAT in FY17 (12 months ended 30 June 2017) was a loss of A$2.6m, an A$0.8m increase on the previous year. Total operating cash burn in FY17 was A$3.3m. The clinical hold on PTX-200 trials saw the cash burn in Q118 decline to A$0.7m vs A$1.0m in Q117. We forecast the expenditure to increase in subsequent quarters as the recruitment in the clinical trials recommences, resulting in a forecast EBITDA loss of A$4.5m in FY18. With clinical trial activity expect to increase in FY19, we forecast an EBITDA loss in that year of A$8.5m. Based on our forecasts, we estimate that Prescient's A$6.9m cash balance at 30 September 2017 will be sufficient to fund operations into FY19. We model that the company will need A$6m in additional cash to fund operations in FY19, which we model as illustrative debt. Depending on the progress the company makes in its clinical development programme, it could potentially obtain additional funds from the exercise of the 58m listed options with an exercise price of 18c that expire in September 2018.

Exhibit 4: Financial summary

A$000s	2015	2016	2017	2018e	2019e
Year end 30 June	AASB	AASB	AASB	AASB	AASB
PROFIT & LOSS					
Revenue	251	992	1,058	645	732
R&D expenses	(986)	(798)	(2,432)	(3,658)	(7,217)
SG&A expenses	(1,398)	(1,959)	(1,359)	(1,365)	(1,862)
EBITDA	(2,133)	(1,765)	(2,733)	(4,539)	(8,495)
Operating Profit (before GW and except.)	(2,133)	(1,765)	(2,734)	(4,539)	(8,504)
Intangible Amortisation	0	0	0	(135)	(129)
Exceptionals	0	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(2,133)	(1,765)	(2,734)	(4,674)	(8,633)
Net Interest	0	11	166	306	135
Profit Before Tax (norm)	(2,133)	(1,754)	(2,568)	(4,234)	(8,369)
Profit Before Tax (IFRS)	(2,133)	(1,754)	(2,568)	(4,368)	(8,498)
Tax benefit	0	0	0	0	0
Profit After Tax (norm)	(2,133)	(1,754)	(2,568)	(4,234)	(8,369)
Profit After Tax (IFRS)	(2,133)	(1,754)	(2,568)	(4,368)	(8,498)
Average Number of Shares Outstanding (m)	49.8	82.2	210.0	211.3	211.3
EPS - normalised (c)	(4.28)	(2.13)	(1.22)	(2.00)	(3.96)
EPS - FRS 3 (c)	(4.28)	(2.13)	(1.22)	(2.00)	(3.96)
Dividend per share (A$)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	3,367	3,368	3,369	3,274	3,176
Intangible Assets	3,367	3,367	3,367	3,232	3,103
Tangible Assets	0	1	2	42	73
Investments	0	0	0	0	0
Current Assets	1,525	10,467	8,861	4,588	2,187
Stocks	0	0	0	0	0
Debtors	216	20	22	22	22
Cash	1,043	9,754	7,645	3,372	972
Other	265	694	1,194	1,194	1,194
Current Liabilities	(439)	(822)	(441)	(441)	(441)
Creditors	(417)	(812)	(401)	(401)	(401)
Short term borrowings	0	0	0	0	0
Other	(22)	(10)	(40)	(40)	(40)
Long Term Liabilities	(2)	(0)	(4)	(4)	(6,004)
Long term borrowings	0	0	0	0	(6,000)
Other long term liabilities	(2)	(0)	(4)	(4)	(4)
Net Assets	4,450	13,013	11,785	7,417	(1,081)
CASH FLOW					
Operating Cash Flow	(2,281)	(1,570)	(3,437)	(4,539)	(8,495)
Net Interest	40	11	159	306	135
Tax	0	0	0	0	0
Capex	0	(1)	(2)	(40)	(40)
Acquisitions/disposals	(525)	4	0	0	0
Financing	0	10,282	1,221	0	0
Dividends	0	0	0	0	0
Other	0	0	(20)	0	0
Net Cash Flow	(2,766)	8,726	(2,079)	(4,273)	(8,400)
Opening net debt/(cash)	(3,809)	(1,043)	(9,754)	(7,645)	(3,372)
HP finance leases initiated	0	0	0	0	0
Other	0	(15)	(29)	0	0
Closing net debt/(cash)	(1,043)	(9,754)	(7,645)	(3,372)	5,028

Source: Edison Investment Research, Prescient Therapeutics accounts

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