EDISON

Viralytics

AACR update

Eye-catching MITCI data

Pharma & biotech

Impressive initial results from the MITCI Phase Ib trial suggest that Viralytics could push to the forefront of the crowded field of immune checkpoint inhibitor (ICI) combination therapies. The first six melanoma patients treated with Cavatak in combination with Yervoy (ipilimumab) experienced a higher response rate (67%) and lower serious adverse event rate (9%) than other prominent ICI combination therapies. These encouraging initial data bode well for the ongoing Phase Ib trials of Cavatak in combination with Merck's Keytruda in melanoma, lung and bladder cancer, and are likely to be of great interest to potential partners. We increase our valuation to A$272m (A$192m previously), or A$1.15 per share (was A$1.04).

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/14	2.5	(4.7)	(3.9)	0.0	N/A	N/A
06/15	2.5	(5.5)	(3.0)	0.0	N/A	N/A
06/16e	4.4	(9.9)	(4.7)	0.0	N/A	N/A
06/17e	4.4	(9.4)	(4.0)	0.0	N/A	N/A

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

Impressive preliminary response rate in MITCI

Preliminary results from the ongoing MITCI Phase Ib trial of Cavatak in combination with Yervoy (ipilimumab) in patients with advanced melanoma were presented at AACR in April. Of the 11 patients treated to date only one (9%) has experienced a serious (grade 3 or higher) adverse event. Four of the six (67%) patients who have been assessed for tumour response have experienced confirmed objective responses (including two complete responses), compared to response rates of 28% and 11% reported for Cavatak and Yervoy, respectively, as single agents and response rates of 56% and 60% for Yervoy in combination with Imlygic (T-vec) and Opdivo. Separately, an update on the CAPRA trial of intra-tumoural injection of Cavatak in combination with the anti-PD1 ICI Keytruda is expected in H216.

Intravenous administration allows broader use

Cavatak can be safely administered intravenously (iv), which gives it a significant advantage over Amgen's approved oncolytic virotherapy Imlygic, which is only suitable for intra-tumoural injection. Viralytics is already collaborating with Merck on the Phase Ib Keynote 200 (STORM part B) trial of iv Cavatak in combination with Keytruda in advanced bladder and lung cancers. Cavatak has already been administered iv in breast, colorectal and prostate cancer patients in Phase I trials, so it could also be tested in combination with ICI drugs in these cancer types.

Valuation: Increased to A$1.15/share

Our risked DCF valuation is increased to A$272m (vs A$192m) or A$1.15/share (vs A$1.04/share) due to higher forecast uptake of Cavatak in melanoma and inclusion of the A$31m net proceeds of the capital raises in December 2015 and January 2016. Cash at 31 March 2016 of A$46.1m is sufficient to fund operations beyond the end of FY18 in our forecasts.

5 May 2016

Price	**A$0.76**
Market cap	**A$180m**
	US$0.76/A$
Net cash (A$m) at 31 March 2016	46.1
Shares in issue	237.3m
Free float	84.6%
Code	VLA
Primary exchange	ASX
Secondary exchange	OTCQX

Share price performance

%	1m	3m	12m
Abs	15.2	0.0	74.7
Rel (local)	9.4	(5.7)	90.4
52-week high/low	A$0.89		A$0.43

Business description

Viralytics is a biopharmaceutical developing Cavatak oncolytic virotherapy to target late-stage melanoma and other solid tumour types. It is trialling Cavatak as a monotherapy and in combination with checkpoint inhibitors. The virus can be delivered iv or by intralesional injection.

Next events

CAPRA Keytruda combo trial update	H216
Further MITCI Yervoy combo trial update	H216
CANON bladder cancer update	H216

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AACR posters confirm potential of Cavatak/ICI combos

Checkpoint inhibitors have markedly improved the treatment prospects for a number of cancers. Responses to the approved ICI drugs Yervoy (ipilimumab), Keytruda (pembrolizumab) and Opdivo (nivolumab) are frequently long-lasting, but response rates to single agent ICI therapy are relatively low, typically in the range 10-30%, meaning that the majority of patients do not respond to ICI therapy. Investigators are seeking combination therapies that can increase the response rates to ICI therapy. For example Merck is undertaking more than 80 trials that combine Keytruda with other cancer treatments. The combination of the two ICI drugs Yervoy and Opdivo has already been approved for use in melanoma, but while 60% of patients responded to therapy, 69% of patients experienced grade 3-4 (serious) adverse reactions.

Cavatak combines a high (20-39%) response rate with a favourable side effect profile when used as a single agent either intravenously or as an intra-tumoural injection, making it an ideal candidate to “prime” or initiate the immune response, which can then be strengthened by combination with ICI therapy, which loosens the host “immunological handbrake”. Merck has already recognised this potential, and is collaborating with Viralytics on the Keynote 200 Phase Ib trial of iv Cavatak in combination with Keytruda in patients with advanced lung and bladder cancer.

Three posters presented at AACR in April provided further evidence of the potential of Cavatak/ICI combination therapy. Selected highlights from the three posters are shown below.

Initial data show high response rate to Cavatak + Yervoy

A poster by Curti et al presented at AACR showed a very encouraging 67% preliminary response rate from the Phase Ib MITCI trial of intra-tumoural Cavatak in combination with the ICI drug Yervoy, which will recruit a total of 26 patients with advanced melanoma.

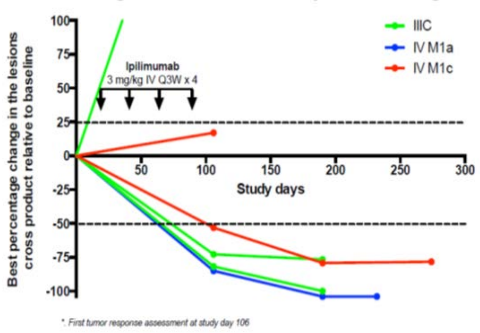
In the trial at least one melanoma lesion was injected with Cavatak four times over a three-week period before treatment with Yervoy commenced, and Cavatak continued to be injected every three weeks for up to a year. Four doses of Yervoy were administered at 3mg/kg iv every three weeks starting at day 22.

Of the 11 patients who have been treated to date, eight had previously undergone systemic immunotherapy. To date, no Cavatak-related grade 3 or higher adverse events have been reported, but there has been one (9%) Yervoy-related grade 3 adverse event (fatigue).

Exhibit 1 shows that four (67%) of the six patients who have reached the first tumour evaluation assessment at day 106 have experienced confirmed objective responses, including two (33%) complete responses. One additional patient with multiple liver metastases who had failed previous therapy with the ICI drugs Yervoy and Keytruda showed stable disease at day 106, bringing the disease control rate to 83%.

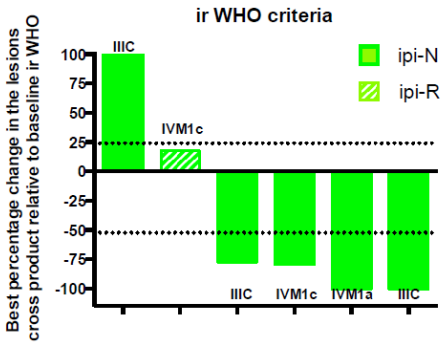
Exhibit 2 summarises the tumour responses of the six patients, while Exhibit 3 shows examples of complete and partial tumour responses.

Exhibit 1: Changes in melanoma tumour burden by disease stage in MITCI trial



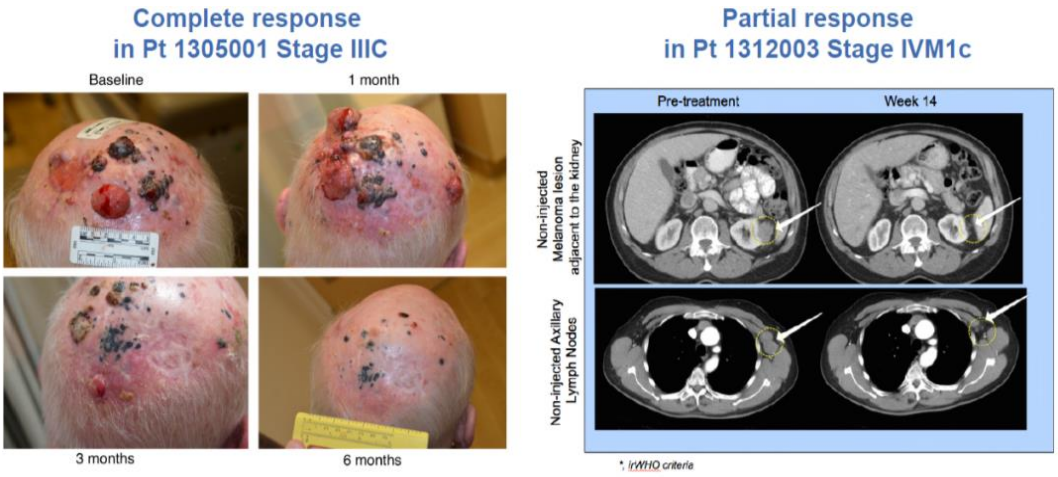
Source: Curti et al poster AACR April 2016

Exhibit 2: Best overall response by ir WHO criteria



Source: Curti et al poster AACR April 2016.
Notes: ipi-N = Yervoy (ipilimumab) naive; ipi-R = resistant to previous Yervoy therapy

Exhibit 3: Example of complete and partial responses in MITCI melanoma trial



Source: Curti et al poster AACR April 2016

While the number of patients with tumour assessments is still quite small, the efficacy data are very encouraging. The 67% Cavatak/Yervoy overall response rate (ORR) is numerically higher than the 60% response rate for the Yervoy/Opdivo combination in melanoma patients in a Phase II trial.

The MITCI response rate is also higher than the 56% (10/18) ORR reported by Puzanov et al at ASCO 2015 for Yervoy combined with Amgen's approve oncolytic virotherapy Imlygic (T-vec). We note that the Puzanov study was in patients who had not undergone any systemic therapy and included patients with less severe stage IIIb disease.

Furthermore the MITCI response rate is higher than the unconfirmed ORR of 56% (n=9/16) in preliminary data reported from the Masterkey-265 study of Imlygic combined with Keytruda. We note that Cavatak has the advantage over T-vec in many other cancer types beyond melanoma in that it can be safely administered iv, whereas T-vec cannot.

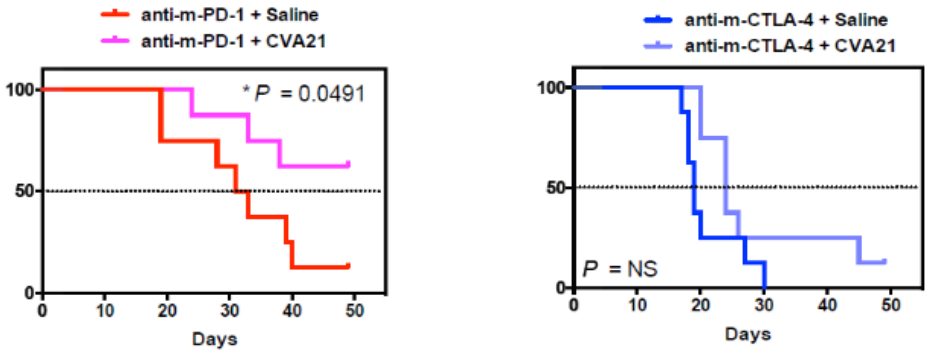
The high response rate and favourable adverse event profile for Cavatak in combination with ICI drugs is expected to attract a high level of interest from potential partners.

Intravenous Cavatak/ICI combo effective in mouse lung cancer model

A poster by Quah et al presented at AACR showed that combining Cavatak with anti-PD1 and anti-CTLA-4 antibodies was more effective at improving survival in a mouse model of lung cancer than either ICI antibody alone (Exhibit 4). This adds to previously presented data showing similar synergy between iv Cavatak and ICI antibodies in a mouse melanoma model and strengthens the rationale underpinning the Keynote 200 clinical trials.

The combination of iv Cavatak with the ICI antibody Keytruda is currently being investigated in non-small cell lung cancer (NSLC) and metastatic bladder cancer patients in the Keynote 200 trial, which is the new name for the Keytruda combination extension of the STORM study. Viralytics is conducting the Keynote 200 study in collaboration with Merck.

Exhibit 4: Adding iv Cavatak to anti-PD1 or anti-CTLA-4 therapy improves survival in an orthotopic mouse model of lung cancer



Source: Quah et al poster AACR April 2016. Note: In this orthotopic mouse model, mouse NSLC tumour cell lines expressing human ICAM1 were growing in the lungs of mice.

CALM immune profiling extension confirms Cavatak stimulates anticancer immune responses in melanoma tumours

The third poster presented at AACR provided an update on the immune-profiling extension of the CALM trial of intra-tumoural injection of Cavatak in melanoma patients. The results show that CAVATAK was able to induce anti-cancer immune activity in the tumour tissue, as shown by the infiltration of immune cells and the up-regulation of key immune checkpoint molecules.

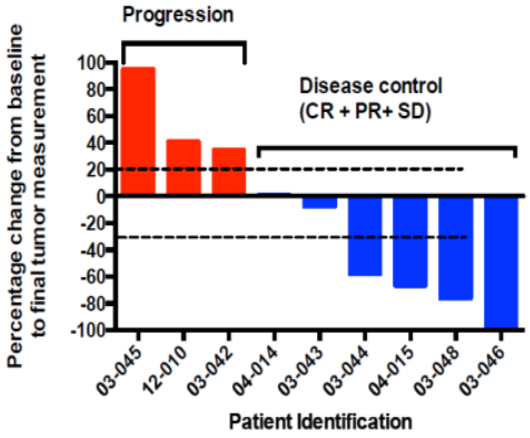
One striking finding of the study was that the changes in immune cell activity were far greater in tumours that responded to therapy than in non-responding tumours.

Exhibit 5 shows the tumour responses in the nine patients with matched sets of biopsies that were analysed in the study. In three patients the injected tumours progressed, shown in red in Exhibit 5. The other six patients where the disease was controlled (stable or shrinking tumours) are shown in blue.

Exhibit 6 shows that the changes within the tumour microenvironment were far greater in the tumours where the disease was controlled following Cavatak administration compared to the tumours that progressed following treatments. These changes in the tumour environment, which occur as early as seven days after the initial administration of Cavatak, could potentially be predictive of tumour response.

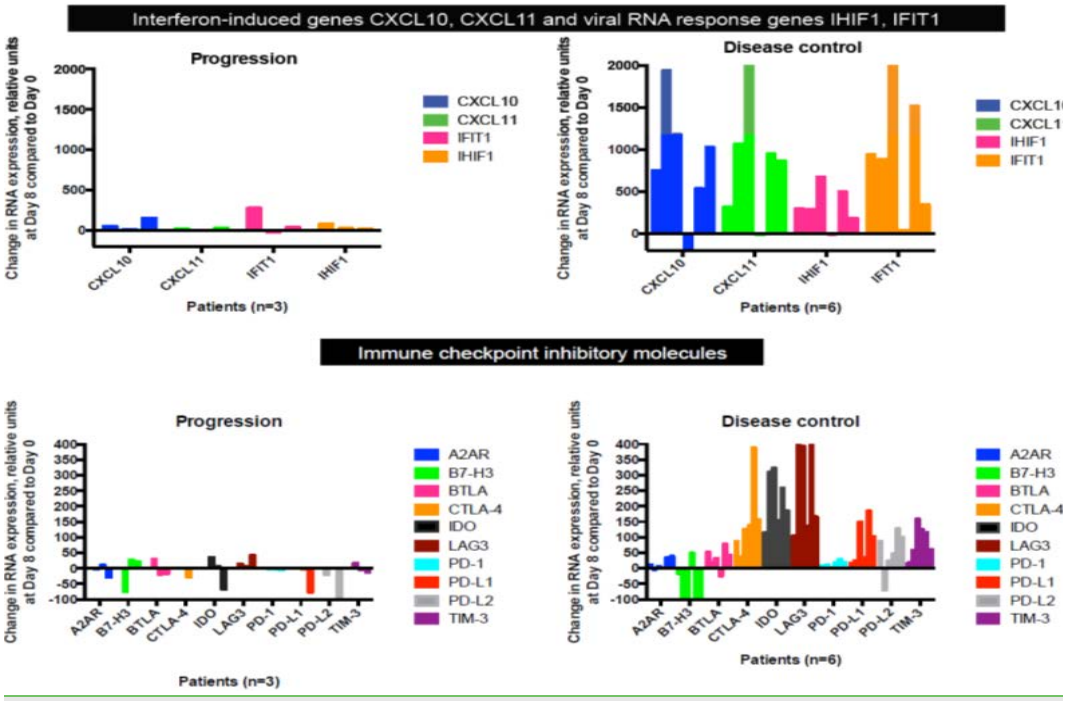
Exhibit 6 also shows that Cavatak treatment up-regulates many immune checkpoint inhibitory molecules in injected melanoma lesions, including CTLA-4, PD-L1, LAG-3, TIM-3 and IDO. Elevated levels of PD-L1 have been associated with improved response rates to the anti-PD1 antibody drugs Keytruda and Opdivo, providing further rationale for the ongoing Cavatak/ICI combination studies.

Exhibit 5: Responses in individual lesions injected with Cavatak in the CALM immune profiling extension study



Source: Andtbacka et al poster AACR April 2016

Exhibit 6: Cavatak up regulates interferon-induced genes and checkpoint inhibitory molecules in melanoma lesions of responder patients



Source: Andtbacka et al poster AACR April 2016

Financials

Viralytics reported total expenses in H116 (period ending 31 December 2015) of A$6.7m, 73% higher than the previous corresponding period (pcp). A$4.5m in R&D expenses were 72% higher than pcp (A$2.6m). With the clinical trial programme continuing to expand, we increase our forecast R&D spend in FY16 and FY17 by 10% to A$11.0m, and SG&A expenses for FY16-FY18 by 41% to A$3.6m. After deducting the R&D rebate, we forecast net R&D expenditure to be A$6.6m for FY16 and FY17, and A$4.8m in FY18. Reported cash at 31 March 2016 was A$46.1m. This gives the company sufficient cash to fund operations beyond our FY18 forecast time frame, based on our forecasts of expenditure.

Valuation

We update our valuation of Viralytics, which now stands at A$272m or A$1.15/share (undiluted, previously A$192m or A$1.04/share). The increase in valuation reflects the ~A$31m net capital raised in December and January (52.7m shares issued at 61.5c/share) and the fact that we have increased forecast uptake of Cavatak in melanoma from 20% to 30% due to the high response rate in preliminary data from the MITCI trial. We have also adjusted the pace at which the 5% penetration rate for NSCLC and bladder cancer drops post peak sales in 2027. We previously had a more rapid decrease but now have modelled in a more gradual drop due to the encouraging trial results.

Our valuation uses a risk-adjusted net present value (rNPV) method to discount future cash flows through to 2033 of the cancer indications shown in Exhibit 7, using a 12.5% discount rate. It assumes a partnering deal or out-licensing of Cavatak in 2017, with the costs of all subsequent clinical development borne by the partner/licensee. 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 (US$25m upfront payment, US$240m total milestones – we assume half of those payments [US$120m] are for clinical and regulatory milestones).

Exhibit 7: Viralytics rNPV valuation

Value driver	Unrisked NPV (A$m)	Probability of success	rNPV (A$m)	rNPV per share (A$)	Key assumptions	
Cavatak in metastatic melanoma	557.0	35%	195.0	0.82	Launch in 2021, with peak market penetration of 30% five years after launch. Peak global sales of US$1.0bn.	Assumes simultaneous product launches in US, Europe and RoW; average price of drug US$75k in US and US$45k elsewhere. One cycle of treatment per patient. Out-licensing in 2016 with all development costs borne by licensee and a 15% royalty on sales due to Viralytics.
Cavatak in NSCLC	369.6	15%	55.4	0.23	Launch in 2023, with peak market penetration of 5% five years after launch. Peak global sales of US$950m.	
Cavatak in CRPC	110.9	15%	16.6	0.07	Launch in 2023, with peak market penetration of 2% five years after launch. Peak global sales of US$285m.	
Cavatak in metastatic bladder cancer	49.7	15%	7.5	0.03	Launch in 2023, with peak market penetration of 5% five years after launch. Peak global sales of US$130m.	
Intravesical Cavatak in NMI bladder cancer	60.4	15%	9.1	0.04	Launch in 2024, with peak market penetration of 10% five years after launch. Peak global sales of US$185m, assuming average price of drug US$10k in US market, and global sales 2x US sales. 15% royalty on sales due to Viralytics.	
Milestones	91.7	50-35%	38.5	0.16	US$25m upfront payment (50% risk adjustment); US$20m milestones on Phase III start, US$40m filing, US$60m on approval (35% risk adjusted).	
R&D expenses (net of rebate)	(9.4)		(5.7)	(0.02)		
Admin	(28.1)	100-10%	(10.4)	(0.04)		
Tax	(301.1)		(76.7)	(0.32)	Australian corporate tax of 30%	
Portfolio Total	900.7		229.3	0.97		
Net cash (end FY16e)			43.0	0.18		
Total			272.3	1.15		

Source: Edison Investment Research

Sensitivities: Trial results and partnering key risks

Viralytics is subject to typical biotech company development risks, including the unpredictable outcome of trials, regulatory decisions, success of competitors, financing and commercial risks. In particular, it has a very high single-product risk, with its entire value residing in Cavatak. The investment case hinges on the outcome of clinical trials and the company's ability to secure a partnership (or further capital) to advance Cavatak into late-stage trials. Ideally, a partner would have the resources to evaluate Cavatak in multiple cancer indications. The greatest commercial

opportunity for Cavatak is likely to be in combination with checkpoint inhibitors or other targeted agents – outcomes of ongoing and planned Phase Ib combination trials could be critical to future clinical and commercial success.

Exhibit 8: Financial summary

A$'000s	2014	2015	2016e	2017e	2018e
30-June	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	2,508	2,454	4,400	4,400	3,200
R&D expenses	(4,998)	(5,925)	(11,000)	(11,000)	(8,000)
SG&A expenses	(2,438)	(2,568)	(3,631)	(3,631)	(3,631)
EBITDA	(4,928)	(6,040)	(10,231)	(10,231)	(8,431)
Operating Profit (before amort. and except.)	(4,956)	(6,074)	(10,286)	(10,300)	(8,514)
Intangible Amortisation	(390)	(390)	(390)	(390)	(390)
Exceptionals	0	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(5,346)	(6,465)	(10,676)	(10,690)	(8,904)
Net Interest	296	527	431	859	671
Profit Before Tax (norm)	(4,660)	(5,547)	(9,855)	(9,441)	(7,844)
Profit Before Tax (FRS 3)	(5,050)	(5,938)	(10,245)	(9,831)	(8,234)
Tax	0	0	0	0	0
Profit After Tax (norm)	(4,660)	(5,547)	(9,855)	(9,441)	(7,844)
Profit After Tax (FRS 3)	(5,050)	(5,938)	(10,245)	(9,831)	(8,234)
Average Number of Shares Outstanding (m)	119.2	184.0	210.7	237.3	237.3
EPS - normalised (c)	(3.9)	(3.0)	(4.7)	(4.0)	(3.3)
EPS - normalised fully diluted (c)	(3.9)	(3.0)	(4.7)	(4.0)	(3.3)
EPS - (IFRS) (c)	(4.2)	(3.2)	(4.9)	(4.1)	(3.5)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	2,523	2,116	1,740	1,349	945
Intangible Assets	2,475	2,034	1,643	1,253	863
Tangible Assets	48	82	96	96	82
Investments	0	0	0	0	0
Current Assets	27,120	24,441	45,842	36,402	28,573
Stocks	0	0	0	0	0
Debtors	2,784	2,875	2,875	2,875	2,875
Cash	24,336	21,566	42,967	33,526	25,697
Other	0	0	0	0	0
Current Liabilities	(767)	(1,685)	(1,685)	(1,685)	(1,685)
Creditors	(767)	(1,685)	(1,685)	(1,685)	(1,685)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	0	0	0	0	0
Long term borrowings	0	0	0	0	0
Other long term liabilities	0	0	0	0	0
Net Assets	28,877	24,872	45,897	36,066	27,832
CASH FLOW					
Operating Cash Flow	(5,486)	(5,010)	(10,363)	(10,230)	(8,430)
Net Interest	0	544	431	859	671
Tax	0	0	0	0	0
Capex	(8)	(69)	(69)	(69)	(69)
Acquisitions/disposals	0	0	0	0	0
Financing	25,180	40	30,973	0	0
Dividends	0	0	0	0	0
Net Cash Flow	19,686	(4,495)	20,972	(9,440)	(7,829)
Opening net debt/(cash)	(5,079)	(24,336)	(21,566)	(42,967)	(33,526)
HP finance leases initiated	0	0	0	0	0
Other	(429)	1,725	429	(0)	0
Closing net debt/(cash)	(24,336)	(21,566)	(42,967)	(33,526)	(25,697)

Source: Edison Investment Research, Viralytics data Note: Risk-adjusted revenue from anticipated licencing deals that have not yet been signed is included in our DCF valuation model but is not included in our financial forecasts.

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