EDISON

Viralytics

Clinical update

Cavatak data continue to impress

Pharma & biotech

Viralytics' Cavatak continues to impress, with a 100% disease control rate in 10 patients (seven objective responses) in combination with Keytruda in the CAPRA Phase Ib study. Furthermore, in the MITCI Phase Ib trial Cavatak, in combination with Yervoy, achieved a 50% response rate in the first 18 patients treated, which is an impressive response rate in a heavily pre-treated population. The encouraging results are a good sign for the ongoing trials of Cavatak and are likely to be of great interest to potential partners. We have increased our anticipated deal value assumptions for Viralytics following recent deals in oncolytic virotherapy, which lifts our valuation to A$385m or A$1.60/share.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/15	2.5	(5.5)	(3.0)	0.0	N/A	N/A
06/16	4.7	(8.0)	(3.8)	0.0	N/A	N/A
06/17e	4.4	(10.2)	(4.3)	0.0	N/A	N/A
06/18e	3.2	(8.6)	(3.6)	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 data from MITCI and CAPRA

Updated results from the ongoing MITCI and CAPRA Phase Ib trials of Cavatak in combination with immune checkpoint inhibitors (ICIs) Yervoy and Keytruda, respectively, were presented at SITC in November 2016. All 10 patients showed a disease control rate in the CAPRA study evaluating intratumoral Cavatak in combination with Keytruda in advanced melanoma; seven of 10 patients (70%) showed an objective response rate and 30% had stable disease. In the MITCI trial, 9/18 (50%) patients with advanced melanoma had objective responses with Cavatak in combination with Yervoy. This compares favourably with reported response rates of 28% for Cavatak, 11% for Yervoy and 33% for Keytruda, as single agents.

Increased deal activity in oncolytic virotherapy

The high response rate and favourable adverse event profile for Cavatak in combination with ICIs is expected to attract a high level of interest from potential partners. There have already been two deals involving oncolytic virotherapy companies so far in 2016. In June 2016 BMS entered an agreement with PsiOxus for trials of its oncolytic virotherapy in combination with nivolumab (Opdivo). The deal included a US$10m upfront fee, but other financial terms were not disclosed. In September 2016 Boehringer Ingelheim entered an option deal with preclinical-stage company Vira Therapeutics that was worth up to €210m (US$236m), including a €20m upfront payment.

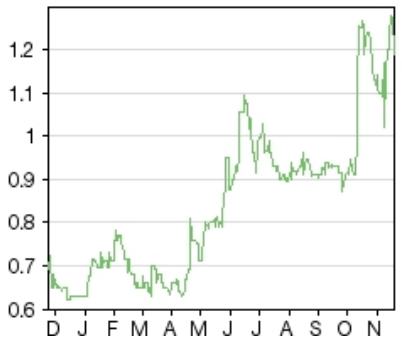
Valuation: Increased to A$1.60/share

Our risked DCF valuation increases to A$385m or A$1.60/share from (A$272m or A$1.15/share) due to an increase in the assumed terms for an anticipated out-licensing deal and rolling forward the DCF model. Cash at 30 September of A$42m is sufficient to fund operations beyond the end of FY18 in our forecasts. We expect the ongoing clinical trials of Cavatak to be of great interest to potential partners.

21 November 2016

Price	**A$1.19**
Market cap	**A$286m**
	US$0.76/A$
Net cash (A$m) at 30 September 2016	42.0
Shares in issue	240.3m
Free float	84.6%
Code	VLA
Primary exchange	ASX
Secondary exchange	OTCQX

Share price performance



%	1m	3m	12m
Abs	(4.8)	28.0	71.2
Reel (local)	(3.7)	32.2	63.7
52-week high/low		A$1.3	A$0.6

Business description

Viralytics is a biopharmaceutical company 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 intravenously or by intralesional injection.

Next events

Further MITCI Yervoy combo trial update	2017
Keynote 200 Keytruda combo update	2017

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Edison profile page

Potentially synergistic Cavatak/ICI combos

Immune checkpoint inhibitor (ICI) drugs have markedly improved the treatment prospects for a number of cancers. Responses to the approved ICI drugs Yervoy (ipilimumab), Keytruda (pembrolizumab), Opdivo (nivolumab) and Tecentriq (atezolizumab) are frequently long-lasting, but response rates to single-agent ICI therapy are relatively low, typically in the range of 10-30%. Viralytics' Cavatak oncolytic virotherapy combines a high (20-39%) response rate with a favourable side effect profile when used as a single agent, either intravenously or as an intratumoral injection, making it an ideal candidate to "prime" or initiate the immune response that 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 and the CAPRA trial combining intratumoral Cavatak with Keytruda in advanced melanoma.

Initial MITCI data show high response rate to Cavatak Yervoy

A poster by Curti et al presented at the 31st Annual Meeting of the Society for Immunotherapy of Cancer (SITC) in National Harbor, Maryland (US) in November 2016 showed an encouraging 50% preliminary response rate from the Phase Ib MITCI trial of intratumoral Cavatak in combination with the ICI 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.

Most of the 18 patients who have been treated to date had previously undergone systemic immunotherapy. To date, no Cavatak-related Grade 3 or higher adverse events have been reported, but there has been one (6%) Yervoy-related Grade 3 adverse event (fatigue).

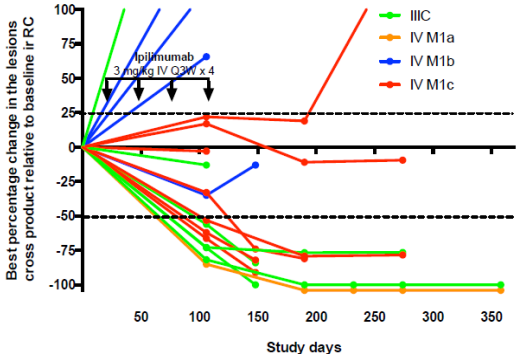
Exhibit 1 shows that nine (50%) of the 18 patients who reached the first tumour evaluation assessment at day 106 experienced confirmed objective responses, including three (18%) complete responses. Five additional patients showed stable disease at day 106, bringing the disease control rate to 78%.

A striking feature shown in Exhibit 1 is that in most cases the tumours continued to shrink long after treatment with ipilimumab stopped.

Exhibit 2 summarises the tumour responses of the 18 patients, while Exhibit 3 shows examples of complete and partial tumour responses.

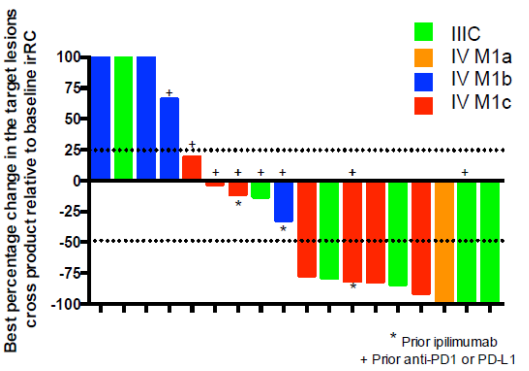
Exhibit 4 shows that there have been three (38%) responses among eight patients who had failed previous treatment with ICI drugs. This is an impressive response rate in patients who have failed to respond to the best available therapies.

Exhibit 1: Changes in melanoma tumour burden by disease stage



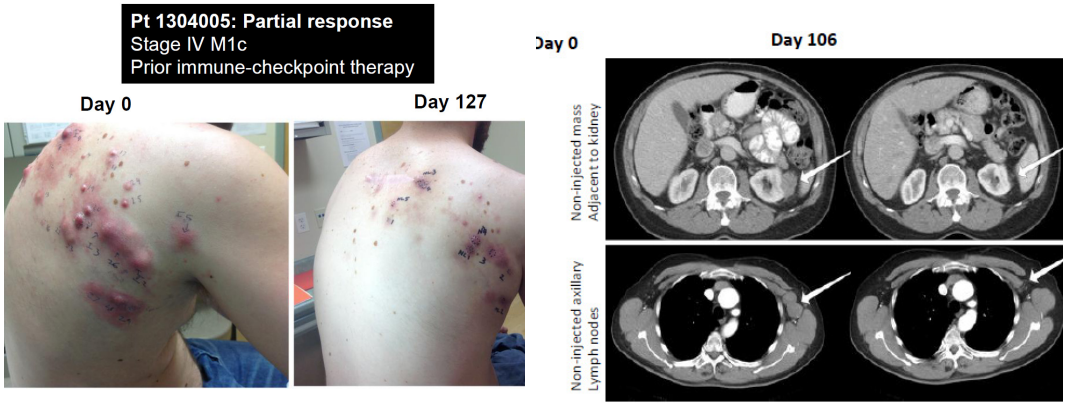
Source: Curti et al poster SITC November 2016. Note: First tumour assessment at day 106.

Exhibit 2: Best overall response by irRC criteria



Source: Curti et al poster SITC November 2016. Note: irRC = immune-related response criteria.

Exhibit 3: Individual patient responses



Source: Curti et al poster SITC November 2016

Exhibit 4: Best overall response in patients with and without prior ICI therapy

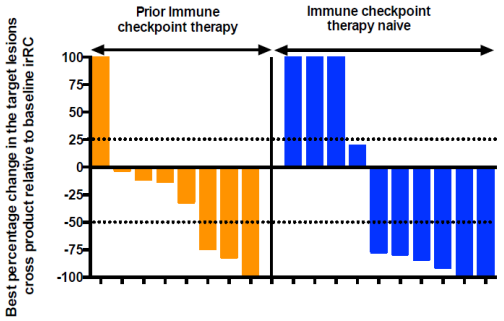
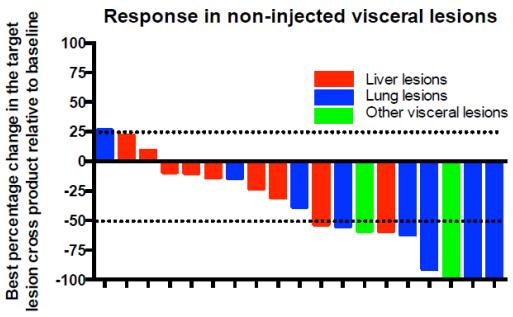


Exhibit 5: Response in non-injected visceral lesions



Source: Curti et al poster SITC November 2016

The efficacy data are very encouraging for a highly pre-treated patient group with advanced melanoma. The 50% Cavatak/Yervoy overall response rate (ORR) is comparable to the 60% response rate for the Yervoy/Opdivo combination in melanoma patients in a Phase II trial.

The MITCI response rate is also comparable to the 56% (10/18) ORR reported by Puzanov et al at ASCO 2015 for Yervoy combined with Amgen's approved 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.

Importantly, there were three responses (38%) among the eight patients who had failed treatment with one or more PD-1 ICI drugs (Exhibit 4). This compares to a response rate of only 10% when

patients who had failed PD-1 ICI drugs were treated with ipilimumab on its own. Furthermore, there were four responses (57%) among the seven patients with Stage IV M1c melanoma with visceral metastases including lung and liver; this included responses in the non-injected visceral lesions.

These preliminary results show that adding Cavatak to an ipilimumab regimen dramatically increased response rates compared to treatment with ipilimumab on its own.

CAPRA combining intralesional Cavatak with pembrolizumab

Viralytics is testing the combination of intralesional Cavatak with pembrolizumab (Keytruda) in advanced melanoma (Stage IIIb/c and IV) in the Phase Ib CAPRA study. The Cavatak dose regimen used in this trial is similar to that in the CALM trial.

The trial uses a Simon's two-stage design. If there are two or fewer responses after 12 months of therapy in the first 12 patients, the trial will be terminated for futility. If there are three or more responses, a further 18 patients will be recruited, taking the total to 30.

Phase Ib data from the first 10 patients presented at SITC showed a disease control rate of 100%. The objective response rate was 70% (7/10) and stable disease was observed in 30% (3/10). These response rates are higher than the published rates for either agent used alone: Cavatak 28% and Keytruda c 33% in patients with late-stage melanoma.

Interestingly, a disease control rate of 100% (7/7 lesions) was observed in individual non-injected visceral and non-visceral lesions, with an objective response rate of 86% (6/7).

Keynote 200 (Storm Part B) well underway

As we described in our previous report, Viralytics has previously presented data from patients administered iv Cavatak in Part A of the Phase I STORM study showing that viral RNA was detected in tumour biopsies of all three melanoma patients, both NSCLC and one of the two bladder patients, but in none of the three prostate cancer patients tested. The expression of viral RNA was also associated with the expression of viral proteins in infected tumour cells.

At SITC, Viralytics presented initial data from the first few patients treated in Part B of the STORM study (Keynote 200), which is being conducted in collaboration with Merck. The study will test iv Cavatak in combination with the anti-PD-1 ICI antibody Keytruda (pembrolizumab) in over 80 patients with advanced NSCLC or metastatic bladder cancer.

Keynote 200 starts by confirming that the three doses of IV Cavatak that were tested as a monotherapy in Part A of the trial are safe to use in combination with pembrolizumab. Six patients of the first two cohorts have been enrolled. Each cohort will test Cavatak doses of $1x10^8$ and $3x10^8$ $TCID_{50}$. Cohort 1 is fully enrolled and enrolment in Cohort 2 is nearing completion. Cohort 3 will treat ~80 patients (~40 NSCLC and ~40 with metastatic bladder cancer) at a dose of $1x10^9$ $TCID_{50}$ after safety is confirmed in the first three patients at this dose.

So far the combination has been well tolerated, with only one unconfirmed Grade 3 treatment-related adverse event and no dose-limiting toxicities for the combination having been reached.

Partnering action

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. Merck is already collaborating with Viralytics in one trial combining Cavatak with pembrolizumab.

There have already been two deals involving oncolytic virotherapy companies so far in 2016. First, in June 2016 BMS entered into an agreement with PsiOxus for trials of its oncolytic virotherapy in

combination with nivolumab (Opdivo). The deal included a US$10m upfront fee, but other financial terms were not disclosed.

Second, in September 2016 Boehringer Ingelheim completed a deal with preclinical-stage company Vira Therapeutics that was worth up to €210m (US$236m). The deal involved an upfront payment of €20m and an option to Boehringer for the right to buy the company on completion of Phase I for €190m. Vira Therapeutics' oncolytic virus is based on the vesicular stomatitis virus (which infects livestock and rodents); the virus is intended to be administered iv in Phase I trials that are expected to commence in 2018.

These deals reflect the belief that oncolytic viruses may provide a complementary mechanism to address tumours that are resistant to ICI therapy because oncolytic viruses are designed to have immune stimulating effects, while ICI drugs are designed to alleviate immune suppression. The high response rates seen with the combination of Cavatak and ipilimumab in the MITCI trial provide strong support for this complementary mechanism.

Valuation

We lift our valuation of Viralytics to A$385m or A$1.60/share (undiluted) from A$272m or A$1.15/share due to increased milestone payment assumptions and rolling forward the DCF model. Our valuation uses a risk-adjusted net present value (rNPV) method to discount future cash flows of the cancer indications shown in Exhibit 6 through to 2033, using a 12.5% discount rate. It assumes a partnering deal or out-licensing 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 and sales milestones from a potential licensing deal, based on average Phase II deal metrics from BioCentury (US$25m upfront payment, US$240m total milestones) and our own assessment of the development stage of Cavatak. We had previously modelled milestone payments of US$120m on the assumption that only half of the payments would be for clinical and regulatory milestones. There is a broad range of value for deals in the oncolytic virus field; from the US$236m Boehringer Ingelheim/Vira Therapeutics deal for a drug that is still in preclinical development, to $1bn ($425m cash upfront and $575m earnout) of the Amgen/BioVex deal for Phase III asset, T-vec. To reflect this, we have increased forecast milestone payments for a Cavatak licence deal from US$120m to US$355m as the product is increasingly generating clinical data, and advancing towards mid-stage development.

Exhibit 6: 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	704.8	35%	246.7	1.03	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	492.7	15%	73.9	0.31	Launch in 2023, with peak market penetration of 5% five years after launch. Peak global sales of US$950m.	
Cavatak in CRPC	148.5	15%	22.3	0.09	Launch in 2023, with peak market penetration of 2% five years after launch. Peak global sales of US$285m.	
Cavatak in metastatic bladder cancer	66.4	15%	10.0	0.04	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	93.8	15%	14.1	0.06	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	272.2	50-35%	104.7	0.44	US$35m upfront payment (50% risk adjustment); US$20m milestones on Phase III start, US$40m filing, US$120m on approval and US$175m sales related milestones (35% risk adjusted).	
R&D expenses (net of rebate)	(10.0)		(6.1)	(0.03)		
Admin	(36.9)	100-10%	(14.1)	(0.06)		
Tax	(394.6)		(102.9)	(0.43)	Australian corporate tax of 30%	
Portfolio total	**1,336.9**		**348.5**	**1.45**		
Net cash (end FY17e)			36.3	0.15		
Total			**384.9**	**1.60**		

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.

Financials

Viralytics reported a total loss of A$9.1m FY16 (year end 30 June) vs A$4.3m in FY15, reflecting increased clinical development activities. We lift forecast SG&A expenditure by A$0.9m to A$4.5m in both FY17 and FY18, in line with the increased expenditure in FY16. We do not include the foreign exchange translation gain or loss in our financial summary (Exhibit 7). Cash at 30 September of A$42m is sufficient to fund operations beyond the end of FY18 in our forecasts.

Exhibit 7: Financial summary

A$'000s	2014	2015	2016	2017e	2018e
30-June	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	2,508	2,454	4,655	4,400	3,200
R&D expenses	(4,998)	(5,925)	(8,604)	(11,000)	(8,000)
SG&A expenses	(2,438)	(2,568)	(4,515)	(4,515)	(4,515)
EBITDA	(4,928)	(6,040)	(8,464)	(11,115)	(9,315)
Operating Profit (before amort. and except.)	(4,956)	(6,074)	(8,501)	(11,170)	(9,371)
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)	(8,891)	(11,560)	(9,761)
Net Interest	296	527	508	922	727
Profit Before Tax (norm)	(4,660)	(5,547)	(7,993)	(10,247)	(8,645)
Profit Before Tax (FRS 3)	(5,050)	(5,938)	(8,383)	(10,637)	(9,035)
Tax	0	0	0	0	0
Profit After Tax (norm)	(4,660)	(5,547)	(7,993)	(10,247)	(8,645)
Profit After Tax (FRS 3)	(5,050)	(5,938)	(8,383)	(10,637)	(9,035)
Average Number of Shares Outstanding (m)	119.2	184.0	212.2	240.3	240.3
EPS - normalised (c)	(3.9)	(3.0)	(3.8)	(4.3)	(3.6)
EPS - normalised fully diluted (c)	(3.9)	(3.0)	(3.8)	(4.3)	(3.6)
EPS - (IFRS) (c)	(4.2)	(3.2)	(3.9)	(4.4)	(3.8)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	2,523	2,116	1,722	1,310	896
Intangible Assets	2,475	2,034	1,643	1,253	863
Tangible Assets	48	82	79	57	33
Investments	0	0	0	0	0
Current Assets	27,120	24,441	50,970	41,175	32,554
Stocks	0	0	0	0	0
Debtors	2,784	2,875	4,849	4,849	4,849
Cash	24,336	21,566	46,121	36,326	27,706
Other	0	0	0	0	0
Current Liabilities	(767)	(1,685)	(2,364)	(2,364)	(2,364)
Creditors	(767)	(1,685)	(2,364)	(2,364)	(2,364)
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	50,328	40,120	31,086
CASH FLOW					
Operating Cash Flow	(5,486)	(5,010)	(8,050)	(11,114)	(9,314)
Net Interest	0	544	508	922	727
Tax	0	0	0	0	0
Capex	(8)	(69)	(33)	(33)	(33)
Acquisitions/disposals	0	0	0	0	0
Financing	25,180	40	30,799	0	0
Dividends	0	0	0	0	0
Net Cash Flow	19,686	(4,495)	23,224	(10,225)	(8,621)
Opening net debt/(cash)	(5,079)	(24,336)	(21,566)	(46,121)	(36,326)
HP finance leases initiated	0	0	0	0	0
Other	(429)	1,725	1,332	429	(0)
Closing net debt/(cash)	(24,336)	(21,566)	(46,121)	(36,326)	(27,706)

Source: Company data, Edison Investment Research

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