Viralytics

ASCO update

Three Cavatak/checkpoint combination trials

Pharma & biotech

Additional data presented at ASCO confirm the potential for synergistic combinations of Cavatak with immune checkpoint inhibitor (ICI) drugs to improve the proportion of cancer patients who respond to ICI therapy. Three Phase Ib trials are underway testing Cavatak in combination with Yervoy or Keytruda in melanoma, lung and bladder cancers. Initial data in April showed an impressive 67% response rate in the first six patients in the MITCI study of Cavatak and Yervoy in melanoma. Further updates on MITCI and initial data from the CAPRA trial of Cavatak plus Keytruda could be potential catalysts for the stock in H216. We maintain our valuation of A$272m (A$1.15 per share) ahead of the anticipated newsflow.

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.

Tumour targeting of iv Cavatak attracted Merck collaboration

Tumour biopsy studies presented at ASCO confirmed successful tumour targeting following iv administration of Cavatak in patients with melanoma, non-small cell lung cancer (NSCLC) and bladder cancer. The immune response to infection of the tumour by Cavatak increased levels of immune cell infiltration and the expression of immune-checkpoint molecules that are targeted by ICI therapies. Viralytics is collaborating with Merck on the recently initiated Phase Ib Keynote 200 (STORM Part B) trial of iv Cavatak in combination with the anti-PD-1 ICI drug Keytruda in advanced bladder and lung cancers.

Updates on ICI combinations in melanoma in H216

Initial data presented in April revealed an impressive 67% response rate in the first six patients treated in the MITCI Phase Ib trial of Cavatak in combination with Yervoy (ipilimumab) in patients with advanced melanoma. We expect further updates on this 26-patient trial in the second half of the calendar year. We also expect an update on the CAPRA trial of intra-tumoural injection of Cavatak in combination with Keytruda in H216. The trial, initiated in September 2015, will recruit 30 patients with advanced melanoma.

Valuation: Unchanged at A$1.15 per share

Our risked DCF valuation is unchanged at A$272m or A$1.15/share. Cash at 31 March 2016 of A$46.1m is sufficient to fund operations beyond the end of FY18 in our forecasts. We expect the ongoing Phase Ib trials of Cavatak in combination with Keytruda in melanoma, lung and bladder cancer to be of great interest to potential partners.

10 June 2016

Price	**A$0.95**
Market cap	**A$225m**
	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	21.0	48.4	6.7
Rel (local)	19.9	42.4	7.6
52-week high/low		A$1.0	A$0.5

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

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

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Potentially synergistic 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), Opdivo (nivolumab) and Tecentriq (atezolizumab) are frequently long-lasting, but response rates to single agent ICI therapy are relatively low, typically in the range 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 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.

Two posters presented at ASCO provided further evidence of the potential of Cavatak/ICI combination therapy. Selected highlights from the posters are shown below.

Successful tumour targeting by iv Cavatak in STORM/Keynote 200 trial

Viralytics presented updated data at ASCO on the detection of Cavatak (CVA21) viral RNA in biopsies of tumour tissue from patients administered iv Cavatak in Part A of the Phase I STORM study. Exhibit 1 shows 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. Exhibit 2 confirms that the expression of viral RNA was also associated with the expression of viral proteins in infected tumour cells.

The expression of viral proteins and the lysis of virus-infected tumour cells both contribute to stimulating an immune response in the tumour micro-environment, including infiltration of the tumour by inflammatory cells.

Exhibit 1: Cavatak viral RNA detected in tumour biopsies after iv administration in STORM Part A study

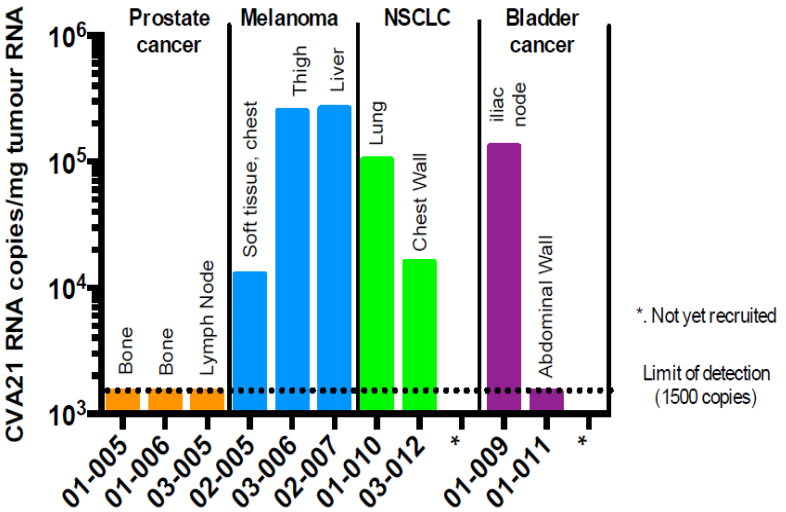
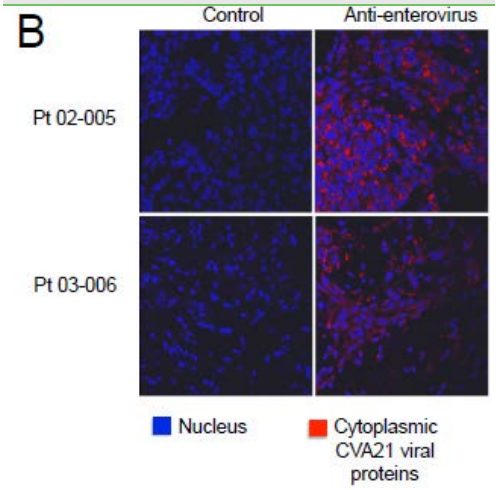


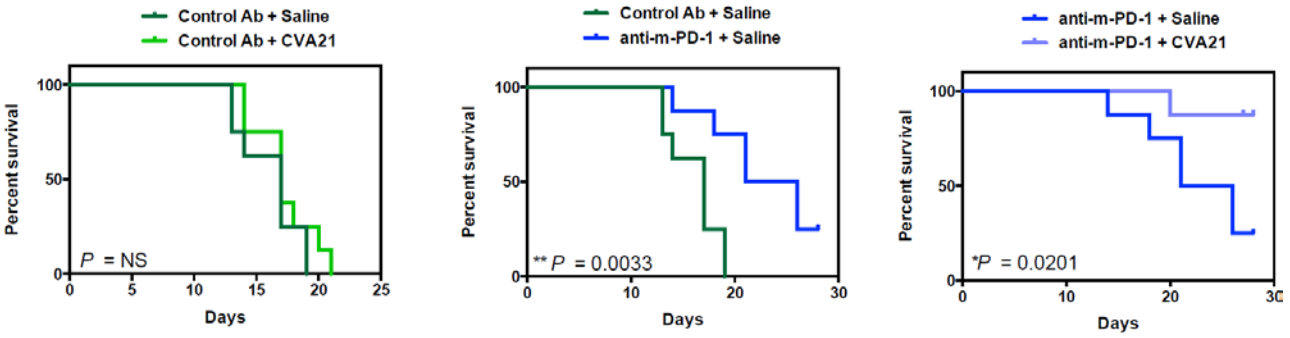
Exhibit 2: Cavatak viral proteins also detected in tumour biopsies



Source: Pandha et al poster #TPS3108 ASCO 2016

The ASCO poster also presented additional data that confirmed the results from previous preclinical studies of Cavatak in combination with an ICI. Exhibit 3 shows that in an immune competent mouse model of NSCLC, combination therapy with iv Cavatak plus a mouse anti-PD-1 antibody significantly increased survival compared to either agent on its own.

Exhibit 3: Combining iv Cavatak with anti-murine-PD-1 monoclonal antibody improves survival in mouse model of non-small cell lung cancer



Source: Pandha et al poster #TPS3108 ASCO 2016

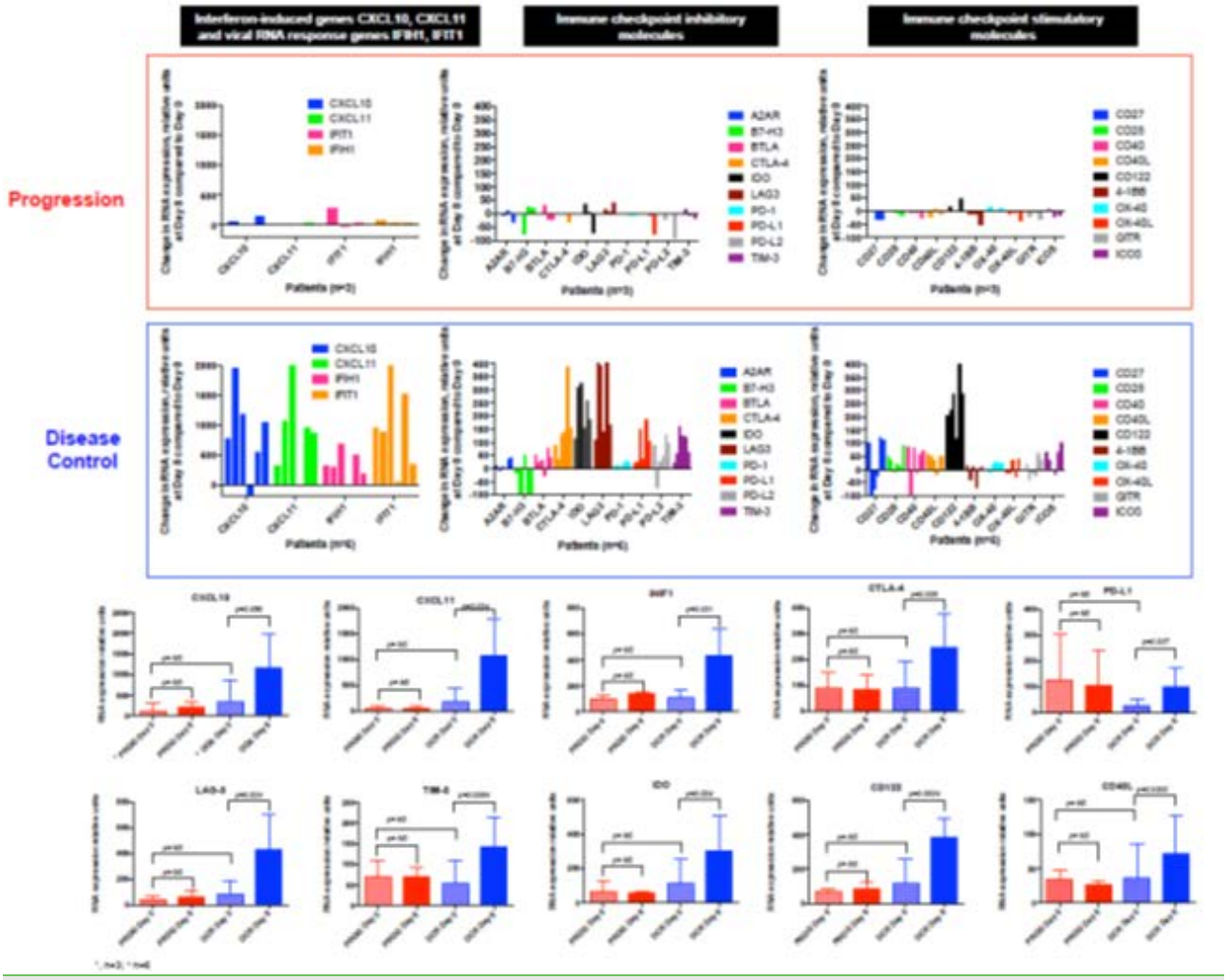
The evidence that Cavatak infects tumour cells in NSCLC and bladder cancer patients following iv administration and the positive outcomes from the preclinical combination studies are both encouraging pointers for potential synergy from the combination in the recently initiated Part B of the STORM study (Keynote 200) being conducted in collaboration with Merck. The study is testing iv Cavatak in combination with the anti-PD-1 ICI antibody Keytruda (pembrolizumab) in 80 patients with advanced NSCLC or metastatic bladder cancer.

CALM immune profiling extension shows statistically significant upregulation of immune response genes

A separate poster at ASCO presented an updated analysis of changes in the tumour micro-environment of melanoma lesions that had been injected with Cavatak, including a detailed comparison of responders vs non-responders.

This provided further evidence that responses to Cavatak therapy were associated with significant upregulation of the expression of genes involved with immune responses. The analysis in Exhibit 4 shows that one week after the first injection with Cavatak (ie day 8), there were statistically significant increases in the expression of at least 10 immune response-related genes in patients who responded to therapy, whereas there were only minimal changes in the expression of these genes in patients who did not respond to therapy and whose disease progressed.

Exhibit 4: Cavatak injection up-regulates interferon-induced genes and immune checkpoint molecules within melanoma tumours



Source: Andtbacka et al poster #9553 ASCO 2016

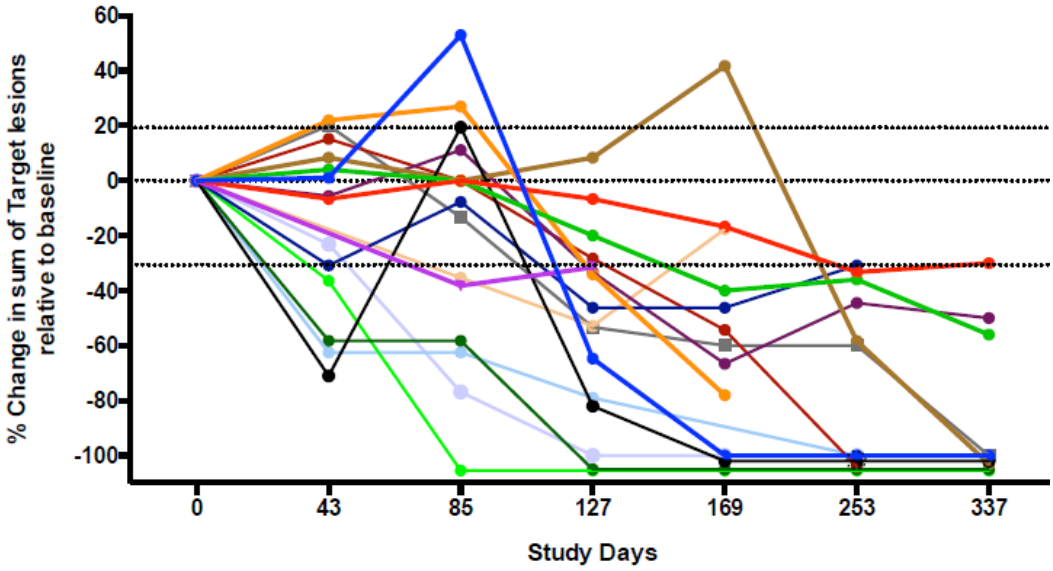
In common with other immunotherapies, Cavatak therapy often leads to delayed tumour shrinkage

Viralytics has previously disclosed that intralesional injection of Cavatak into melanoma lesions in the CALM Phase II trial resulted in an overall response rate (ORR) of 28% (16/57) and a durable response rate of 21%.

Exhibit 5 shows the change in total measured tumour burden over time in the 16 responders in the CALM trial. In common with other cancer immunotherapy treatments, several patients experienced delayed responses to treatment. Five of the 16 responders, including three of the eight complete responders, had increases in tumour burden of at least 20% within the first six months of the study before eventually responding to treatment. This initial increase in tumour burden followed by tumour shrinkage is known as pseudoprogression. It can be caused by a delayed onset of the immune response, or by an initial increase in the size of tumours due to infiltration by inflammatory cells and the swelling (oedema) associated with the inflammatory response, with subsequent tumour shrinkage as the inflammation subsides.

In the Cavatak clinical trials tumour responses are assessed using modified criteria known as irRECIST, which include an allowance for a temporary increase in tumour burden.

Exhibit 5: Changes in tumour burden of responding patients in CALM Phase II



Source: Andtbacka et al poster #9553 ASCO 2016

Valuation

Our valuation of Viralytics is unchanged at A$272m or A$1.15/share (undiluted). 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 6, 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 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	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 7: 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 licensing 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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