EDISON

Viralytics

Clinical trial update

Cavatak Phase II meets primary end point

Pharma & biotech

The US Phase II CALM study of intratumoural Cavatak in advanced melanoma has met its primary end point early, with a promising 33% response rate. The study remains on track for full enrolment in Q413 and should render final data by end-2014. Positive CALM data paves the way for a randomised Phase II study in late-stage melanoma and should increase partnering interest. Separately, the Phase I/II STORM study of intravenous Cavatak in advanced solid tumours is expected to start in Q413 following UK regulatory approval. Our valuation remains at A$61m.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/11	1.4	(2.1)	(3.7)	0.0	N/A	N/A
06/12	0.9	(4.3)	(6.4)	0.0	N/A	N/A
06/13	2.5	(3.7)	(4.5)	0.0	N/A	N/A
06/14e	1.7	(4.9)	(5.6)	0.0	N/A	N/A

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

Phase II CALM study meets end point early

The US, single-arm Phase II CALM study of intratumoural (IT) Cavatak, as monotherapy in patients with late-stage (IIIc and IV) melanoma, has met its primary end point early with an encouraging immune related Progression Free Survival (irPFS) rate of 33% (10 out of first 30 evaluable patients). Moreover, the CALM data suggest that multiple dosing with IT Cavatak is well tolerated, with relatively mild adverse events (grade 1 or 2) and no serious AEs. CALM has now enrolled 44 patients and should reach its target of 54 evaluable patients by end 2013. Although final data are awaited (late 2014), the positive early readout supports progression into a randomised Phase II study and should increase partnering interest.

UK regulatory nod for Phase I/II STORM

Viralytics has received approval from the UK Medicines and Healthcare products Regulatory Agency (MHRA) to initiate the two-stage Phase I/II STORM study of intravenous (IV) Cavatak in 30 patients with advanced solid tumours (melanoma, prostate, lung, bladder). Starting in Q413, the Phase I stage will administer Cavatak as monotherapy, while the second Phase II part will combine Cavatak with standard chemotherapy (docetaxel or carboplatin/paclitaxel) in the most responsive cancer type identified in Phase I. We expect the study to render initial data in 2014, which, if positive, could see Cavatak being developed further in other solid cancers.

Valuation: A$0.69/share (undiluted)

Our base case valuation of Viralytics remains unchanged at A$61m, or A$0.69/share (undiluted), derived using a risk-adjusted net present value method in only the lead indication of metastatic melanoma, and end-June 2014 net cash of c A$200k. We currently assume a 30% (Phase II) probability of success for IT Cavatak in melanoma. There is potential upside to our base case valuation if IV Cavatak delivers positive STORM data and, thus, is developed for a range of cancers other than melanoma.

24 September 2013

Price	**A$0.38**
Market cap	**A$33m**

Net cash (A$m) as at end-June 2013	5.1
Shares in issue	87.3m
Free float	100%
Code	VLA
Primary exchange	ASX
Secondary exchange (*ADR = 3 ordinary shares)	OTCQX*

Share price performance

%	1m	3m	12m
Abs	20.6	58.3	49.0
Rel (local)	17.6	42.6	25.9

52-week high/low	A$0.47	A$0.22

Business description

Viralytics is an ASX-listed biopharmaceutical developing virus applications using a common cold producing virus to target late-stage melanoma. The Phase II CALM trial is evaluating intratumoural administration of lead candidate Cavatak in patients with metastatic melanoma.

Next events

Start STORM trial	H213
Complete enrolment for CALM trial	December 2013

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Viralytics datasheet

Exhibit 1: R&D programmes (active and pending)

Product	Mode of administration	Indication	Stage	Development notes
CAVATAK	Intratumoural	Melanoma	Phase II	Phase II CALM study in malignant melanoma (n=63, final read-out end 2014). Monotherapy. Phase II CALM extension study with dosing up to 48 weeks in total.
	Intravenous	Mel, breast, lung, prostate	Phase II	Phase I/II STORM trial planned in H213 in two stages (test indication, Chemo-combo).
	Intratumoural	Head and neck	Phase I	On hold. Phase I head and neck cancer complete.
	Intratumoural	Prostate	Preclinical	On hold. Oncolytic activity in xenograft tumour models in mice.
	Intratumoural	Glioma	Preclinical	On hold. Oncolytic activity in athymic mice bearing malignant glioma tumours.
	Intravenous	Pancreatic	Preclinical	On hold. Oncolytic activity in xenograft tumour models in mice.
	Intravenous	Multiple myeloma	Preclinical	On hold. Promising data from study in multiple myeloma (MM) cell lines.
		Bladder	Discovery	On hold. Signs of synergy of CVA21 and radio/chemotherapy in bladder cell lines.
		Mesothelioma	Discovery	On hold. ICAM-1 over-expressed by cultured cells of all mesothelioma cell lines.
EVATAK		Ovarian	Preclinical	On hold. Therapeutic dose-response demonstrated in SCID mouse model.
		Prostate	Preclinical	On hold. Therapeutic dose-response demonstrated in SCID mouse model.
		Gastric	Preclinical	On hold. Therapeutic dose-response demonstrated in SCID mouse model.

Source: Edison Investment Research. Note: SCID = Severe combined immunodeficiency.

Exhibit 2: Approved treatment for malignant melanoma

Product	Company	Mechanism of action	Notes
Zelboraf (vemurafenib)	Roche	BRAF inhibitor	FDA (2011)/EU (2012) approved for unresectable or metastatic melanoma in patients with the BRAF V600E mutation.
Yervoy (ipilimumab)	BMS	T-cell mediated immune response	FDA (2011)/EU (2011) approved for unresectable or metastatic melanoma.
Tafinlar (dabrafenib)	GSK	BRAF inhibitor	FDA approved (May 2013) for unresectable melanoma or metastatic melanoma in adult patients with BRAF V600E mutation.
Mekinist (trametinib)	GSK	MEK inhibitor	FDA approved (May 2013) for unresectable or metastatic melanoma in adult patients with BRAF V600E or V600K mutation.

Source: Edison Investment Research

Exhibit 3: Competing development programmes for malignant melanoma

Product	Company	Mechanism	Development stage/notes
TVEC (talimogene laherparepvec/ OncoVEXGM-CSF)	Amgen	Oncolytic virus	439-pt Phase III trial comparing intratumoural TVEC to subcutaneous GM-CSF in previously treated unresectable Stage IIIb/c and IV melanoma. Results: met primary end point of durable response rate (DRR: rate CR or PR lasting continuously for ≥6 months). Statistically significant difference in DRR: 16% in the TVEC arm vs 2% in the GM-CSF arm. OS analysis, a secondary end point, is event driven; interim analysis showed an OS trend in favour of TVEC as compared to GM-CSF. The OS data are expected to mature in H114.
Ipilimumab	BMS	Immunotherapy	950-pt Phase III trial vs placebo after complete resection of high-risk Stage III melanoma. Results: Q213.
			700-pt Phase III trial of ipilimumab at 3mg/kg vs 10mg/kg in metastatic melanoma. Results: Q415.
Nivolumab /ipilimubab	BMS	Immunotherapy	915-pt Phase III trial of nivolumab vs nivolumab + ipilimumab vs ipilimumab in previously untreated unresectable or metastatic melanoma. Results: Q416.
Nivolumab	BMS	Immunotherapy	410-pt Phase III trial of nivolumab vs dacarbazine in previously untreated, unresectable or metastatic melanoma. Results: Q415.
			390-pt Phase III trial of nivolumab vs dacarbazine, carboplatin or paclitaxel in advanced melanoma progressing post anti-CTLA-4 therapy. Results: Q215.
Vemurafenib	Roche	BRAF inhibitor	3,300-pt Phase III trial in surgically resected, BRAF mutant metastatic melanoma. Results: Q215.
			725-pt Phase III trial in resected, BRAF mutant melanoma at high risk for recurrence. Results: Q316.
Vemurafenib/ GDC-0973	Roche	BRAF/MEK inhibitor	500-pt Phase III trial of vemurafenib ± GDC-0973 in untreated BRAF mutant unresectable advanced or metastatic melanoma. Results: Q316.
Dabrafenib	GSK	BRAF inhibitor	200-pt Phase III trial of dabrafenib vs dacarbazine (DTIC) in previously untreated BRAF mutant advanced (Stage III) or metastatic (Stage IV) melanoma. Results: Q313.
Dabrafenib/ trametinib	GSK	BRAF/MEK inhibitor	694-pt Phase III trial of dabrafenib + trametinib to vemurafenib in BRAF mutant unresectable (Stage IIIc) or metastatic (Stage IV) melanoma. Results: Q214.
			340-pt Phase III trial of dabrafenib + trametinib vs dabrafenib first-line in BRAF mutant unresectable (Stage IIIc) or metastatic (Stage IV) melanoma. Results: Q213.
MEK162	Novartis	MEK inhibitor	393-pt Phase III trial of MEK162 vs dacarbazine in KRAS mutant advanced unresectable or metastatic melanoma. Results: Q414.
LGX818	Novartis	BRAF inhibitor	900-pt Phase III trial of LGX818 ± MEK162 vs vemurafenib in BRAF mutant melanoma. Results: Q217.
Lambrolizumab	Merck	Anti PD-1	510-pt Phase II trial of lambrolizumab vs chemotherapy (carboplatin + paclitaxel, paclitaxel alone, dacarbazine or temozolomide) in advanced melanoma after previous therapy.

Source: Edison Investment Research

Update: CALM study meets primary end point

The Phase II CALM trial is a single-arm, open-label, multi-centre US study evaluating intratumoural (IT) injections of Cavatak, administered as monotherapy in patients with advanced melanoma. The trial has met its primary end point early and is expected to deliver final data in H214:

- The primary end point of CALM is stable disease (or better) at six months after the first dose of Cavatak, as measured by irPFS. The irPFS response of at least 10 patients was achieved after the first 30 evaluable patients. There are now 44 patients enrolled and the trial is on track to meet full enrolment target of 54 evaluable patients by end-2013. The irPFS measure was chosen based on prognostic benchmarks developed in a meta-analysis of 42 Phase II trials in metastatic melanoma and recognises the lag in therapeutic response inherent in immunotherapy treatments.
- Secondary end points of the CALM study include: durable response rate (DRR), one-year survival, overall survival (OS), disease control rate, safety and tolerability.

Final readout for the CALM study is expected in H214. Positive initial results from the Phase II CALM trial supports Viralytics' plan to move IT Cavatak into a randomised Phase II study and should support partnering/licensing discussions. Clinical settings for a randomised Phase II study of Cavatak could include monotherapy, as treatment prior to surgery or in combination with other new frontline therapies.

Intravenous Cavatak Phase I/II STORM study to commence in the UK

Viralytics has received final approval from the MHRA to undertake its two-stage Phase I/II STORM (Systemic Treatment Of Resistant Malignancies) study in patients with late-stage melanoma, prostate, lung and metastatic bladder cancer. The lead study investigators are oncologists: Professor Hardev Pandha (University of Surrey), Professor Kevin Harrington (The Institute of Cancer Research and The Royal Marsden, London) and Professor Alan Melcher (St James's University Hospital, Leeds).

Stage one (Phase I) of the study will evaluate the impact of intravenous administration of Cavatak in a range of cancers including melanoma, prostate, lung and metastatic bladder, in order to identify the most responsive cancer type/indication for Stage two. The second stage (Phase II) will then focus on the 'preferred' cancer identified in Phase I and investigate multiple intravenous dosing of Cavatak in combination with standard chemotherapy (docetaxel or carboplatin/paclitaxel). With approval now granted for commencement in H213, STORM should render initial data in 2014. Proof of efficacy of Cavatak administered intravenously, if established, could broaden the potential commercial applications of the drug to other solid tumour indications beyond melanoma.

Sensitivities

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 the entirety of its value residing in Cavatak. The investment case hinges on the outcome of the CALM study and, assuming data are positive, the company's ability to secure a partnership (or further capital) to advance Cavatak into late-stage trials. Ideally, a partner would have an established oncology franchise with the resources and experience to evaluate Cavatak in multiple cancer indications. Another key sensitivity is the rapidly evolving treatment landscape for melanoma, which means that future trials of Cavatak will likely be in combination with targeted agents and/or immunotherapies – selection of the appropriate therapy to combine with Cavatak could be critical to future clinical and commercial success.

Valuation

We value Viralytics at A$61m, or A$0.69/share (undiluted), using a risk-adjusted net present value method to discount future cash flows through to 2032 in metastatic melanoma only. Our approach assumes a partnering deal or out-licensing of Cavatak post-release of the final Phase II data in 2014, with all costs of subsequent clinical development borne by the partner/licensee. Of note, our model does not include upfront payments or milestones from a potential licensing deal. Product launch is assumed in 2020 with peak market share of 20% in 2024, representing peak sales of US$646m, before tapering off for the remaining term of market exclusivity under the Biologic Licence Approval of 12 years. A 30% probability of success has been applied to reflect Cavatak's phase of clinical development with projected cash flows discounted at 12.5%. There is additional upside to our base case valuation since Cavatak could be developed for a range of cancers other than melanoma, given positive preclinical data and the prospect of new indications identified in the upcoming STORM trial.

Financials

The company reported A$2.5m in R&D tax deferred credits related to its clinical development costs in FY12 and FY13, of which A$1.9m relates to FY13. Deferred tax credits under the Australian R&D tax incentive scheme provide a 45% cash rebate in the following fiscal year and are recognised as revenue. Net cash at year end was A$5.1m. Cash burn is expected to remain c A$1.2m per quarter for FY14e given operating cash outflows in Q413 of A$1.2m, which included R&D expense of A$0.8m, with a cash runway extending to mid-2014 and that coincides with the expected CALM study readout. We have adjusted our FY14 and FY15 forecasts for deferred R&D tax credits to reflect both FY13 actual R&D costs of c A$4m and projected FY14 R&D costs of c A$5m. If a partner or licensee is not secured for Cavatak, Viralytics intends to conduct a further Phase II trial, which could require additional capital of between A$10m and A$20m. However, given the positive signs of efficacy to date and the potential of a significant readout, the prospects for attracting a pharma licensing partner appear promising.

Exhibit 4: Financial summary

A$'000s	2010	2011	2012	2013	2014e
30-June	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	0	1,406	875	2,493	1,706
Cost of Sales	0	0	0	0	0
Gross Profit	0	1,406	875	2,493	1,706
EBITDA	(3,664)	(2,246)	(4,621)	(3,912)	(5,093)
Operating Profit (before amort. and except.)	(3,765)	(2,302)	(4,659)	(3,934)	(5,123)
Intangible Amortisation	(390)	(390)	(390)	(390)	(390)
Exceptionals	(20)	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(4,175)	(2,693)	(5,049)	(4,324)	(5,513)
Net Interest	23	240	317	257	254
Profit Before Tax (norm)	(3,742)	(2,063)	(4,342)	(3,678)	(4,869)
Profit Before Tax (FRS 3)	(4,152)	(2,453)	(4,732)	(4,068)	(5,259)
Tax	0	0	0	0	0
Profit After Tax (norm)	(3,742)	(2,063)	(4,342)	(3,678)	(4,869)
Profit After Tax (FRS 3)	(4,152)	(2,453)	(4,732)	(4,068)	(5,259)
Average Number of Shares Outstanding (m)	362.3	55.3	67.5	81.5	87.3
EPS - normalised (c)	(1.0)	(3.7)	(6.4)	(4.5)	(5.6)
EPS - normalised and fully diluted (c)	(1.0)	(3.7)	(6.4)	(4.5)	(5.6)
EPS - (IFRS) (c)	(1.1)	(4.4)	(7.0)	(5.0)	(6.0)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	N/A	N/A	N/A
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET					
Fixed Assets	4,077	3,675	3,267	2,931	2,551
Intangible Assets	3,998	3,607	3,217	2,863	2,473
Tangible Assets	79	68	50	68	78
Investments	0	0	0	0	0
Current Assets	5,463	6,365	7,039	7,281	2,402
Stocks	137	365	0	0	0
Debtors	200	995	1,154	2,202	2,202
Cash	5,126	5,005	5,884	5,079	200
Other	0	0	0	0	0
Current Liabilities	(925)	(981)	(746)	(1,235)	(1,235)
Creditors	(613)	(664)	(746)	(1,235)	(1,235)
Short term borrowings	(312)	(317)	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	8,614	9,058	9,560	8,978	3,719
CASH FLOW					
Operating Cash Flow	(3,811)	(3,190)	(3,561)	(3,934)	(5,093)
Net Interest	219	159	5	0	254
Tax	0	0	0	0	0
Capex	(4)	(49)	(20)	(40)	(40)
Acquisitions/disposals	506	0	0	0	0
Financing	6,899	2,959	4,455	3,169	0
Dividends	0	0	0	0	0
Net Cash Flow	3,810	(121)	880	(806)	(4,879)
Opening net debt/(cash)	(1,049)	(4,814)	(4,688)	(5,884)	(5,079)
HP finance leases initiated	0	0	0	0	0
Other	(45)	(5)	317	0	0
Closing net debt/(cash)	(4,814)	(4,688)	(5,884)	(5,079)	(200)

Source: Edison Investment Research, Viralytics accounts

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