EDISON

CytRx

Pipeline report

Detailed results on aldoxorubicin presented

Pharma & biotech

Detailed results of the Phase IIb trial of aldoxorubicin in first-line STS patients presented at the annual meeting of ASCO (top-line results were reported in several press releases) continue to show the drug's superior efficacy and safety profile over doxorubicin. The 400-patient, FDA SPA-sanctioned Phase III trial in second-line STS is progressing well with targeted completion of accrual in 2015 and possible top-line readout in 2016, a major value inflection point if the data are positive.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/12	0.1	(18.9)	(0.82)	0.0	N/A	N/A
12/13	0.3	(23.4)	(0.71)	0.0	N/A	N/A
12/14e	0.0	(35.7)	(0.71)	0.0	N/A	N/A
12/15e	0.0	(43.9)	(0.86)	0.0	N/A	N/A

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

Detailed Phase IIb aldoxorubicin results

Investigators of the Phase IIb trial of aldoxorubicin in first-line soft tissue sarcoma (STS) presented the baseline, safety and efficacy data of the trial at the annual meeting of ASCO held from 31 May to 2 June in Chicago. The additional data on response, in particular the percentage of patients with any tumour shrinkage, not only continue to demonstrate aldoxorubicin's superiority over doxorubicin, but also showed that doxorubicin had resulted in tumour shrinkage by central lab review. Previously the central lab review recorded 0% of response for doxorubicin because these tumour shrinkages failed to meet the partial response cut-off, and the result caused some concern among investors as doxorubicin has historically achieved some, albeit modest, response in STS. In our opinion, this new disclosure should have calmed the fear that doxorubicin underperformed, and therefore, aldoxorubicin's superior efficacy was questionable in the Phase IIb trial.

Events to watch in 2014

Results that should affect the stock include preliminary data from the Phase II GBM trial and overall survival (OS) of the Phase IIb first-line STS. Positive OS data from the Phase IIb present a high bar because of the trial's relatively small size. We should note that the primary endpoint of the SPA-sanctioned Phase III second-line STS trial is PFS, not OS.

Valuation: $438m suggests upside potential

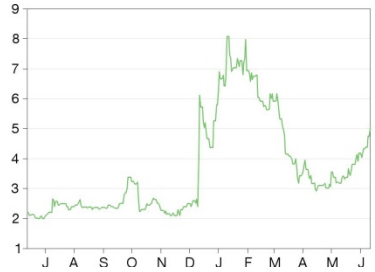
We have updated our risk-adjusted NPV of CytRx to $438m or $8.67/share (previously $466m), with the principal change being our decreased forecast of the cash position at the end of 2014 and 2015, reflecting increased R&D cost estimates after Q114 actual results.

12 June 2014

Price	**US$5.0**
Market cap	**US$280m**

Net cash ($m) 31 March 2014	112.6
Shares in issue	56.06m
Free float	87%
Code	CYTR
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	57.9	1.2	127.1
Rel (local)	52.5	(2.8)	90.0
52-week high/low	US$8.0	US$2.0	

Business description

CytRx is a US biopharmaceutical company focused on oncology. The company's novel technology platform (albumin-binding linkers) provides targeted delivery of chemotherapy to tumours. Lead programme aldoxorubicin is in Phase III for second-line STS and currently in Phase II for GBM and Kaposi's sarcoma.

Next events

Start of Phase II in second-line SCLC	Q314
Preliminary data from Phase II GBM trial	H214
OS data from Phase IIb first-line STS	H214

Analysts

Jason Zhang PhD	+1 646 653 7027
Dr Mick Cooper	+44 (0)20 3077 5734

healthcare@edisongroup.com

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Aldoxorubicin Phase IIb detailed data

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Exhibit 1: Phase IIb first-line STS trial results

	Aldoxorubicin		Doxorubicin	
Treatment	Aldoxorubicin, 350mg/m^2, (260mg/m^2 dox equiv.), Every 3wk up to 6 cycles		Doxorubicin, 75mg/m^2, Every 3wk up to 6 cycles	
N	83		40	
ECOG, (%)				
0-1	96%		92%	
2	4%		8%	
Histology:				
Leiomyosarcoma	34%		35%	
Liposarcoma	16%		15%	
Fibrosarcoma	14%		10%	
Synovial sarcoma	6%		10%	
Other	30%		30%	
Safety: (grade 3/4 treatment emerging adverse events)				
Neutropenia	40%		20%	
Neutropenic fever	16%		18%	
Thrombocytopenia	6%		5%	
Anaemia	13%		20%	
Nausea/vomiting	7%		0%	
Mucositis	11%		3%	
Fatigue/weakness	6%		5%	
# with >10% decrease in LVEF	24%		33%	
# with >15% decrease in LVEF	10%		24%	
# with ≤50% of expected institutional normal	0%		6%	
Efficacy:	Investigator		Central lab	
	Aldoxorubicin	Doxorubicin	Aldoxorubicin	Doxorubicin
PFS, mths	8.4	4.7	5.7	2.8
p value	0.0004		0.014	
HR	0.419 (0.25-0.69)		0.584 (0.37-0.93)	
p value	0.0007		0.024	
PFS at 6 mths	68.1%	36.6%	45.7%	22.9%
p value	0.002		0.020	
Overall response:				
CR	2.4%	0.0%	0.0%	0.0%
PR	19.3%	5.0%	23.8%	0.0%
ORR	21.70%	5%	23.8%	0.0%
Any tumour shrinkage	**64.5%**	**41.2%**	**60.8%**	**39.4%**

Source: Company reports and ASCO 2014

Financials

CytRx reported net income in Q114 of $4.7m, compared with a net loss of $6.9m in Q113, mainly because of a recognised non-cash gain of $14.7m on the valuation of warrant derivative liabilities related to warrants issued in August 2011 and July 2009. R&D expenses for the quarter were $7.0m, including $4.9m for aldoxorubicin, compared to $3.2m for Q113. The company ended the quarter, which included the net $81m February equity raise, with cash, cash equivalents and short-term investment of $112.6m.

We have updated our financial model, mainly to increase R&D cost estimates based on Q114 actual results and the company's guidance on trial progress. We now estimate R&D expenses in 2014 and 2015 will be $33.5m and $36.9m, respectively, compared to $22.7m and $25m, previously. We continue to estimate that the cash on hand should support the company's operation into 2016.

CytRx datasheet

Exhibit 2: CytRx's R&D pipeline summary

Product	Indication	Stage	Notes
Aldoxorubicin	Second-line soft tissue sarcoma (STS)	Phase III	400-pt Phase III, SPA-sanctioned study of aldoxorubicin vs physician's choice of five chemotherapy regimens in relapsed, or refractory STS. OS is primary endpoint. Aldoxorubicin allowed to be dosed to progression. Trial started in March 2014.
		Phase I	25-pt Phase Ib/IIa study included 13 advanced STS patients tested at the maximum tolerated dose (MTD) (350mg/m^2): showed partial response in 39%, stable disease in 54%, clinical benefit in 77%, median PFS of 11.3 months and OS of 21.7months, no acute cardiotoxicity and acceptable safety and tolerability at doses equal to 3.5x the standard doxorubicin dose.
	First-line STS	Phase IIb	123-pt trial of 350mg/m^2 of aldoxorubicin (n=83) or 75mg/m^2 doxorubicin (n=40) every three weeks for up to six cycles with metastatic, locally advanced or unrespectable STS. Reported PFS of 8.4 mths vs 4.7 mths (investigator assessed, or IA, p=0.0002); Hazard ratio (HR) of 0.37 (95% CI 0.212 to 0.643, p=0.0004); 5.7 mths vs 2.8 mths (central lab review, or CLR, p=0.018), HR of 0.59 (95% CI 0.36 to 0.96, p=0.034). Six-month PFS 67.1% vs 36.1% (p=0.005, IA) and 46.8% vs 23.7% (p=0.038, CLR). Final ORR is 25.4% vs 5.4% (IA) and 23% vs 0% (CLR).
	Second-line glioblastoma multiforme (GBM)	Phase II ready	FDA approval for 28-pt Phase IIb trial in recurrent GBM following first-line chemotherapy (temozolomide). Currently enrolling patients, with preliminary results targeted for Q314. Positive preclinical data in animal model of GBM.
	AIDS-related Kaposi's sarcoma	Phase II	Up to 30-pt Phase II study started in Q114. Standard of care is liposomal doxorubicin (Doxil), but this is often sub-optimal due to toxicity and/or a lack of clinical response.
	Second-line SCLC	Phase IIb	Planned 132-pts Phase IIb trial comparing aldox or topotecan (randomised 1:1). Trial to start in Q314.
	First-line STS	Phase Ib/II	Up to 30 pts trial testing the combination of aldox and ifosfamide; planned to start in Q314.
	Metastatic solid tumour	Phase Ib/II	Up to 30 pts trial testing the combination of aldox and gemcitabine: planned to start in Q314

Source: Edison Investment Research

Exhibit 3: Competing STS therapies in Phase III development

Product (company)	Setting	Population	Design/primary endpoint	Expected read-out	Notes
Aldoxorubicin (CytRx)	Second-line	Relapsed/refractory or intolerant to previous chemo	400-pt study of aldoxorubicin vs physician's choice. Primary endpoint: OS.	2016	Covered by SPA, Started in Q114.
TH-302 (Threshold)	First-line	Locally advanced, unresectable or metastatic	620-pt study of doxorubicin ± TH-302. Primary endpoint: OS.	H115	Covered by SPA. Interim OS analysis in H114, final OS data in H115.
Eribulin (Eisai)	Second-line	Locally advanced, unresectable or metastatic L-sarcoma	450-pt study of eribulin vs dacarbazine. Primary endpoint: OS.	H115	L-sarcoma includes liposarcoma or leiomyosarcoma; failed first-line anthracycline.
Trabectedin (Zeltia/J&J)	Second-line	Locally advanced, unresectable or metastatic L-sarcoma	570-pt study of trabectedin vs dacarbazine. Primary endpoint: OS.	H114	L-sarcoma subtypes only; failed first-line anthracycline.

Source: Threshold Pharmaceuticals, Zeltia, Edison Investment Research

Exhibit 4: Selected Phase III efficacy results in STS

Product (company)	Setting	Treatment regimen	Study	No (n)	Median PFS (mths)	CR (%)	PR (%)	SD (%)	Clinical benefit (%)	Reference
Aldoxorubicin (CytRx)	First-line	Monotherapy	Phase IIb	123	8.4	2.4	19.3	N/A	N/A	ASCO 2014
	Second/third-line		Phase I/II	13	6.4	0	39	54	93	Chawla et al, ASCO 2012
Doxorubicin	First-line	Monotherapy	Phase IV	167	4.3	7	18	45	70	Nielsen et al, Sarcoma 2000
			Phase IV	455	4.6	0	13	46	59	EORTC 62012, ESMO 2012
Votrient (GSK)	Second-line	Monotherapy	Phase III	369	4.6	0	4	N/A	-	Prescribing information
TH-302 (Threshold)	First-line	Combo with doxorubicin	Phase I/II	91	6.7	2	34	48	84	Phase II, CTOS 2012

Source: CytRx, Sarcoma J, CTOS, ESMO, ASCO, GSK. Note: CR=complete response, PR=partial response, SD=stable disease.

Exhibit 5: Financial summary

$000s	2011	2012	2013	2014e	2015e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	250	100	300	0.0	0.0
Cost of Sales	0	0	0	0	0
Gross Profit	250	100	300	0	0
R&D Expenses	15,491	12,685	17,500	33,538	36,892
SG&A Expenses	7,317	8,353	10,274	8,981	9,071
EBITDA	(21,958)	(18,985)	(23,489)	(35,888)	(43,963)
Operating Profit (before amort and except)	(22,006)	(19,042)	(23,549)	(36,018)	(44,083)
Intangible Amortisation	(48)	(57)	(60)	(3,250)	(2,000)
Exceptionals	7,915	2,767	(20,210)	14,703	0
Other	(395)	(1,762)	(3,802)	(3,210)	(1,900)
Operating Profit	(14,534)	(18,094)	(47,622)	(27,776)	(47,983)
Net Interest	207	132	138	300	200
Profit Before Tax (norm)	(21,799)	(18,910)	(23,412)	(35,718)	(43,883)
Profit Before Tax (FRS 3)	(14,327)	(17,962)	(47,484)	(27,476)	(47,783)
Tax	(98)	(2)	0	0	0
Profit After Tax (norm)	(21,692)	(18,721)	(23,229)	(35,679)	(43,783)
Profit After Tax (FRS 3)	(14,425)	(17,964)	(47,484)	(27,476)	(47,783)
Average Number of Shares Outstanding (m)	17.9	23.0	32.9	50.5	51.0
EPS - normalised (c)	(120.9)	(81.5)	(70.6)	(70.6)	(85.8)
EPS - normalised fully diluted (c)	(120.9)	(55.1)	(48.8)	(62.4)	(75.9)
EPS - (IFRS) (c)	(80.4)	(78.2)	(144.4)	(54.4)	(93.6)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	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	573	539	476	339	212
Intangible Assets	184	184	184	184	184
Tangible Assets	266	253	175	38	(89)
Investments	123	102	117	117	117
Current Assets	37,282	39,666	41,024	86,527	42,771
Stocks	0	0	0	0	0
Debtors	176	110	117	31	31
Cash	36,047	38,344	38,568	84,296	40,540
Other	1,059	1,212	2,338	2,200	2,200
Current Liabilities	(13,600)	(10,066)	(30,839)	(16,797)	(16,797)
Creditors	(6,861)	(6,094)	(6,656)	(7,318)	(7,318)
Deferred revenue	(6,739)	(3,972)	(24,182)	(9,479)	(9,479)
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	24,255	30,139	10,662	70,068	26,186
CASH FLOW					
Operating Cash Flow	(16,671)	(19,045)	(22,704)	(35,384)	(43,963)
Net Interest	0	0	138	300	200
Tax	0	0	0	0	0
Capex	(53)	(135)	0	7	7
Acquisitions/disposals	6,938	0	0	0	0
Financing	18,940	21,477	24,095	80,805	0
Dividends	0	0	0	0	0
Other	0	0	0	0	0
Net Cash Flow	9,154	2,297	1,528	45,728	(43,756)
Opening net debt/(cash)	(26,892)	(36,047)	(38,344)	(38,568)	(84,296)
HP finance leases initiated	0	0	0	0	0
Other	1	0	(1,304)	0	0
Closing net debt/(cash)	(36,047)	(38,344)	(38,568)	(84,296)	(40,541)

Source: Company accounts, Edison Investment Research

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
US

Sydney +61 (0)2 9258 1161
Level 25, Aurora Place
88 Phillip St, Sydney
NSW 2000, Australia

Wellington +64 (0)48 948 555
Level 15, 171 Featherston St
Wellington 6011
New Zealand