EDISON

Onconova Therapeutics

Quarterly update

Important ONTIME disclosure

Pharma & biotech

Onconova clarified on its Q413 call that the subgroup in which rigosertib showed a statistically significant survival benefit over BSC was predefined for secondary analysis, adding more credibility to the benefit seen and raising the possibility of a conditional approval for this substantial group of higher-risk MDS patients. The company plans to meet the FDA and EU regulator in Q214 and provide a regulatory update. Onconova ended 2013 with cash of $100m, enough to support its operation beyond 2014.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/12	46.2	(30.3)	(15.51)	0.0	N/A	N/A
12/13	4.8	(62.2)	(6.05)	0.0	N/A	N/A
12/14e	4.0	(65.1)	(2.96)	0.0	N/A	N/A
12/15e	4.0	(67.2)	(2.99)	0.0	N/A	N/A

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

Subgroup predefined

Onconova confirmed that the subgroup in which rigosertib demonstrated a statistically significant overall survival (OS) benefit over best supportive care (BSC) was predefined in the trial's protocol. Pre-definition of a subgroup adds more credibility to the benefit that is seen with the treatment as compared to the so-called "post-hoc" analysis. Because the benefit was clinically meaningful (a median OS difference of 3.8 months with an HR of 0.67 and a p-value of 0.022) and this substantial group of patients (those who progressed on or failed to respond to previous treatment with hypomethylating agents (HMAs) accounted for c 62% of all patients enrolled) have the poorest prognosis, we believe there is a possibility that rigosertib could gain conditional approval in the US based on this data, with a commitment of confirmatory Phase III trial.

ASCO presentation will shed more light on the data

Onconova will present pre-clinical data at the AACR annual meeting from 5-9 April in San Diego that supports the drug's new mechanism of action, which is under-appreciated by the market, in our opinion. Data from the Phase III ONTIME trial will be presented at the upcoming ASCO annual meeting from 30 May to 3 June in Chicago. Detailed data such as response rate and post-trial treatment differences may help explain why the drug succeeded in the non-responder subgroup but failed in the intend-to-treat (ITT) population, building a scientific case for the FDA to consider an approval of the drug for the subpopulation.

Valuation: Near-term upside with rigosertib update

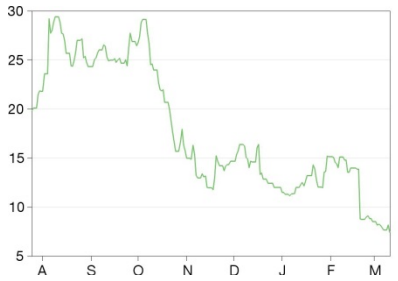
Our valuation of the company is $311m, or $14.5/basic share, which is increased slightly from our previous valuation at $303m based on higher estimated 2014 year end cash. Our pipeline value remains at $272m with a 50% probability of success of rigosertib in higher-risk MDS. A conditional approval of the drug based on the benefit seen in ONTIME would increase the value to $426m, or $19.9 per share.

12 March 2014

Price	**US$7.44**
Market cap	**US$159m**

Net cash ($m) at end 2013	100
Shares in issue	21.4m
Free float	21%
Code	ONTX
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(47.5)	(46.9)	N/A
Rel (local)	(48.8)	(49.3)	N/A
52-week high/low	US$29.4	US$7.4	

Business description

Onconova Therapeutics is a clinical-stage biopharmaceutical company focused on developing novel small molecule drug candidates to treat cancer. Its lead drug candidate, rigosertib, is partnered with Baxter (Europe) and SymBio (Japan/Korea) and is in a Phase III trial for higher-risk mylodysplastic syndrome (MDS) (IV form), and in Phase II for lower-risk MDS (oral form).

Next events

ONTIME data presentation	ASCO
Rigosertib higher risk MDS reg. update	Q214
Initiation of oral rigosertib lower risk MDS pivotal trial (SPA)	H214
Start of Phase II of oral rigosertib + azacitidine in first-line MDS	H214

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Onconova datasheet

Exhibit 1: Onconova pipeline summary

Drug	Indication	Status	Notes
Rigosertib	Higher-risk MDS after HMA (IV)	Top-line results announced: missed primary endpoint; subgroup analysis suggests OS benefit in HMA non-responders, a predefined subgroup.	Licensed to **Baxter** (total earnable payments of $600m) for Europe, and **SymBio** (total earnable payments of $50m) for Japan/Korea. Onconova retains all rights elsewhere (including in the US). Temple University is entitled to 25% of sub-licence fees from Baxter and SymBio and a low single-digit royalty on net sales.
	Lower-risk MDS (oral)	Phase II final results at ASH	
	Refractory head and neck cancer (oral)	Phase II single arm, first results: 2014	
ON 013105	Refractory lymphoma, solid tumours	Phase I (solid tumour)	Cyclin D1 targeting agent. Studies could resume in Q114.
Recilisib	Acute radiation syndrome	Phase I ongoing	Collaboration with the US Department of Defense for radiation-induced cytopenia. Expected to be licensed out early.

Source: Edison Investment Research. Notes: Only clinical-stage assets shown.

Exhibit 2: Ongoing rigosertib clinical trials

Trial name	Patients	Treatment	Details
ONTIME (04-21)	MDS, Vidaza or Dacogen failure	Rig (CI, 3-d Q2W for eight cycles or Q4W after eight cycles) plus BSC vs BSC alone	299-pt Phase III shows median OS of 8.2 vs 5.8 months, HR= 0.86, p=0.27. Post hoc analysis suggests OS benefit in HMA non-responders (median OS of 8.5 vs 4.7 months, HR of 0.67, p=0.022).
ONTARGET (09-05)	MDS, TD, low, Int-1 or trisomy 8 Int-2	Oral, 560mg bid for two weeks Q3W	60-pt Phase II, single arm, primary endpoint: units of blood cell transfusions at week eight. Start: May 2012, results: Oct 2014.
09-08	MDS, AML and CML	Oral, various doses bid for three weeks Q4W; plus Vidaza	40-pt Phase I/II, primary endpoints: safety. Trial start: Aug 2013. Results: Aug 2015.
09-09	Squamous cell carcinoma, refractory	Oral, 560mg bid for two weeks Q3W	80-pt Phase II, primary endpoint: ORR; trial start: March 2013. Results: Sept 2015.
09-07	MDS, transfusion dependent, low, Int-1	Oral, 560mg bid for two weeks Q3W	40 pt Phase II, primary endpoints: HI. Trial start: July 2013. Results: June 2015.
04-24 (ONTIME)	MDS, failure after Vidaza or Dacogen, excess blasts	CI, 1,800mg/m^2 for three days Q2W (eight cycles) or Q4W (after eight cycles)	90 pt Phase IIIB, primary endpoint: relationship between bone marrow response and survival. Start: Aug 2013. Results Dec 2015.

Source: Edison Investment Research, Clinicaltrials.gov. Note: CI = confidence interval; Q2W: every two weeks.

Exhibit 3: Competitive environment – approved or developmental drugs for lower- and higher-risk MDS

Drug	Company	Mechanism of action	Main indication	Status	Route of admin	Selected relevant data in higher- and lower-risk MDS	Reference
Vidaza (azacitidine)	Celgene	HMA	High risk MDS	Approved in all major countries	IV and SC		N/A
Dacogen (decitabine)	Eisai/Astex	HMA	High risk MDS; elderly AML	Approved in US for MDS, EU for elderly AML	IV	Phase I, n=36 Int-2/high MDS failed Vidaza, 7/36 (19.4%) ORR, incl. 3mCR and 2SD, med. OS 7.3 months	ASH 2013 Abs# 2796
Revlimid	Celgene	IMiDs	Low risk, 5q-; MM	Approved worldwide	Oral	Phase II plus pred., n=25 low/Int-1, non-5q- MDS, 5/23 (22%) RBC TI	ASH 2013 Abs# 1506
SGI-110	Otsuka/Astex	HMA	New or ref. MDS, AML	Phase II	SC	n=93, 74 AML, 19 MDS, 2 CR, 1CRp and 2CRi in AML; 2mCR, 3 HI-E, 1 HI-N and 1 HI-P in MDS (prior HMA)	ASH 2013 Abs# 1548
ARRY-614	Array Biopharma	p38 MAPK and Tie2 inhibitor	Low/Int-1 MDS	Phase I	Oral, qd or bid	n=62, 12/54 evaluable and 9/31 on drug >16 weeks had HI	ASH 2013 Abs# 387
Sapacitabine	Cyclacel Pharma	Nucleoside analogue	Elderly MDS ref. to HMA	Phase II randomised	Oral, qd or bid	n=63; 2 CR, 2 CRp, and 5 major HI; med. OS 8.6-9.7 months	ASH 2013 Abs# 2752
Clolar (clofarabine)	Sanofi/ Genzyme	Second-gen nucleoside analogue	rr ALL, AML etc	Approved for rr ALL	IV daily x5	Phase II w/ cytarabine, n=29, 8/24 (33%) CR/CRp/mCR, 4/24 (17%) had SD, med. OS 4.8 months	ASH 2013 Abs# 1525
Pracinostat (SB939)	MEI Pharma	HDAC inhibitor	New AML and MDS	Phase II	Oral, thrice weekly (TIW)	In pilot Phase II, MDS, w/aza, 7/9 (CR+CRi+PR) incl 7 CR	ASH 2012 ABS# 3821
Telintra (TLK199)	Telik	Glutathione S-transferase Inh.	Lower risk MDS	Phase II	Oral	n=38 low/Int-1 MDS, 11 of 38 (29%) had HI-E; 3 of 11 (27%) had TI	Cancer. 2012, 118:2138-2147
Oral azacitidine (CC-486)	Celgene	HMA	Maintenance Rx in AMLw/ CR	Phase III	Oral	n=53 low/Int-1 MDS; 18/53 (34%) ORR, 13/53 (24.5%) HI, 12/30 (40%) TI>56 d, 7/30 (23.3%) TI>84 d	ASH 2012 Abs# 424
Mocetinostat	Mirati Therapeutics	HDAC inhibitor	Int-2/high MDS	Phase I/II	Oral	n=66 AML and MDS, w/aza., 22 MDS (13/22 (59%, CR+CRi), 6/17 (35%) TI	ASH 2013 Abs# 1550
Vosaroxin	Sunesis Pharm.	Nucleoside analogue	AML or MDS	Phase I/II	IV	Data in MDS pending	N/A

Source: Edison Investment Research. Note: IMiDs = immunomodulatory drugs.

Valuation

We have updated our valuation of Onconova after the Q413 results. The pipeline valuation remains the same with a clinical success probability of 50% and 35% for second-line, higher-risk MDS and lower-risk MDS, respectively. Peak sales for rigosertib IV for second-line, high-risk MDS is $305m, and oral rigosertib for lower risk MDS is $1bn. This approach yields an intrinsic value of $272m for the pipeline. Adding forecast year-end 2014 cash of $39m yields a total value of $311m, equivalent to $14.5 per basic share ($13.8 per diluted share). Previously, we had valued Onconova at $303m, or $14.1 per basic share ($13.5 per diluted share).

Exhibit 4: Onconova valuation model

Product	Main indication	Status	Probability of success	Launch year	Peak sales ($m)	Patent protection	Royalty	rNPV ($m)
Rigosertib (IV)	2nd-line MDS, higher risk	Phase III	50%	2016	305	2026	Fully own in US; low teens to high 20s for EU	$115
Rigosertib (oral)	MDS, lower risk, non-5q-	Phase II	35%	2017	1,036	2026		$136
ON 013105	Head & neck	Phase I	25%	2019	149	>2026	Fully own	$11
Recilisib	Acute radiation syndrome	Phase I		N/A			To be licensed out	$10
Total								$272

Cash and cash equivalents (YE14) ($m)	39.0
Total firm value ($m)	311
Total basic shares (m)	21.4
Value per basic share ($)	14.5
Stock options (2014, m)	2.8
Weighted average exercise price ($)	8.5
Cash on exercise ($m)	23.8
Total firm value ($m)	335
Total number of shares	24.2
Diluted value per share ($)	13.8

Source: Edison Investment Research

Financials

Onconova reported a net loss of $14.6m for Q413, including G&A expenses of $4.4m and R&D costs of $12.1m. Cash burn for the quarter was $7.1m. The total loss for the year was $62.2m, including G&A expense of $16.8m and R&D expense of $50.2m. Cash burn for the year was $61m. The company ended 2013 with cash and cash equivalents of $100m. We have changed our 2014 forecast slightly based on actual Q413 results and we now estimate the company's cash utilisation will be $61.3m in 2014 and it will end the year with cash of $39m, assuming no rigosertib-related milestone payment in 2014. We previously estimated cash utilisation of $68m in 2014 and year-end cash of $31m.

Exhibit 5: Financial summary

$m	2011	2012	2013	2014e	2015e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	1.5	46.2	4.8	4.0	4.0
Cost of Sales	0.0	0.0	0.0	0.0	0.0
Gross Profit	1.5	46.2	4.8	4.0	4.0
EBITDA	(27.9)	(44.7)	(71.0)	(73.5)	(75.7)
Operating Profit (before amort. and except.)	(27.6)	(22.3)	(62.2)	(65.1)	(67.2)
Intangible Amortisation	0.0	0.0	0.0	0.0	0.0
Exceptionals	1.3	0.4	0.0	0.0	0.0
Other	0.0	0.6	0.1	0.0	0.0
Operating Profit	(26.3)	(21.3)	(62.1)	(65.0)	(67.2)
Net Interest	(0.0)	(8.6)	(0.0)	(0.0)	(0.0)
Profit Before Tax (norm)	(27.6)	(30.3)	(62.2)	(65.1)	(67.2)
Profit Before Tax (FRS 3)	(26.3)	(29.9)	(62.1)	(65.0)	(67.2)
Tax	0.0	0.0	0.4	0.0	0.0
Profit After Tax (norm)	(27.6)	(30.3)	(61.7)	(65.1)	(67.2)
Profit After Tax (FRS 3)	(26.3)	(29.9)	(61.7)	(65.0)	(67.2)
Average Number of Shares Outstanding (m)	2.14	2.21	10.59	22.00	22.50
EPS - normalised ($)	(14.79)	(15.51)	(6.05)	(2.96)	(2.99)
EPS - normalised and fully diluted ($)	(14.79)	(15.51)	(6.05)	(2.96)	(2.99)
EPS - (IFRS) ($)	(12.30)	(13.55)	(5.82)	(2.96)	(2.99)
Dividend per share (p)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0	100.0
EBITDA Margin (%)	(1877.3)	(96.7)	(1493.6)	(1837.3)	(1891.5)
Operating Margin (before GW and except.) (%)	(1854.3)	(48.2)	(1309.1)	(1626.7)	(1680.9)
BALANCE SHEET					
Fixed Assets	0.6	0.6	0.8	1.0	1.4
Intangible Assets	0.0	0.0	0.0	0.0	0.0
Tangible Assets	0.6	0.6	0.8	1.0	1.4
Investments	0.0	0.0	0.0	0.0	0.0
Current Assets	3.8	83.3	104.4	39.0	2.8
Inventory	0.0	0.0	0.0	0.0	0.0
Accounts receivable, net	0.0	0.0	0.0	0.0	0.0
Cash and cash equivalents	2.7	81.5	100.0	39.0	2.8
Other	1.1	1.7	4.4	0.0	0.0
Current Liabilities	(12.1)	(25.4)	(10.3)	(10.1)	(9.9)
Creditors	(12.1)	(25.4)	(10.3)	(10.1)	(9.9)
Short term borrowings	0.0	0.0	0.0	0.0	0.0
Long Term Liabilities	(10.8)	(15.5)	(13.9)	(9.9)	(5.9)
Deferred revenue, long term	(10.7)	(15.4)	(13.9)	(9.9)	(5.9)
Other long term liabilities	(0.1)	(0.0)	(0.0)	(0.0)	(0.0)
Net Assets	(18.4)	43.0	80.9	20.0	(11.7)
CASH FLOW					
Operating Cash Flow	(14.2)	1.6	(60.7)	(61.3)	(63.5)
Net Interest	(0.0)	0.0	(0.0)	(0.0)	(0.0)
Tax	0.0	0.0	0.0	0.0	0.0
Capex	(0.2)	(0.3)	(0.4)	(0.3)	(0.3)
Acquisitions/disposals	0.0	0.0	0.0	0.0	0.0
Financing	9.8	77.5	79.7	0.5	27.5
Dividends	0.0	0.0	0.0	0.0	0.0
Net Cash Flow	(4.6)	78.8	18.5	(61.1)	(36.2)
Opening net debt/(cash)	(7.3)	(2.7)	(81.5)	(100.0)	(39.0)
HP finance leases initiated	0.0	0.0	0.0	0.0	0.0
Other	0.0	0.0	(0.1)	0.0	0.0
Closing net debt/(cash)	(2.7)	(81.5)	(100.0)	(39.0)	(2.8)

Source: Company reports, Edison Investment Research

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