7th November 2016

Healthcare

Actelion

Price CHF137.10

Macitentan successful in MERIT phase II trial in CTEPH

Fair Value CHF180 (+31%) **NEUTRAL**

Bloomberg	ATLN VX
Reuters	ATLN.VX
12-month High / Low (CHF)	173.8 / 122.5
Market Cap (CHFm)	14,774
Ev (BG Estimates) (CHFm)	13,856
Avg. 6m daily volume (000)	365.0
3y EPS CAGR	5.5%

	1 M	3 M	6 M	31/12/15
Absolute perf.	-18.4%	-16.8%	-11.0%	-1.8%
Healthcare	-7.9%	-12.6%	-5.9%	-16.3%
DJ Stoxx 600	-3.4%	-1.2%	-1.2%	-9.4%

YEnd Dec. (CHFm)	2015	2016e	2017e	2018e
Sales	2,042	2,344	2,263	2,390
% change		*14.8%*	*-3.5%*	*5.6%*
EBITDA	769	908	766	835
EBIT	655.6	788.1	644.9	713.0
% change		*20.2%*	*-18.2%*	*10.6%*
Net income	693.5	832.1	708.2	772.6
% change		*20.0%*	*-14.9%*	*9.1%*

	2015	2016e	2017e	2018e
Operating margin	40.7	45.6	42.1	45.2
Net margin	34.0	35.5	31.3	32.3
ROE	52.6	45.1	31.4	28.2
ROCE	77.0	88.4	84.7	98.9
Gearing	-30.7	-49.7	-63.5	-72.0

(CHF)	2015	2016e	2017e	2018e
EPS	6.17	7.64	6.57	7.23
% change	-	*23.9%*	*-14.1%*	*10.1%*
P/E	22.2x	17.9x	20.9x	19.0x
FCF yield (%)	4.2%	4.9%	4.9%	5.1%
Dividends (CHF)	1.50	1.50	1.50	1.50
Div yield (%)	1.1%	1.1%	1.1%	1.1%
EV/Sales	7.0x	5.9x	5.9x	5.4x
EV/EBITDA	18.7x	15.3x	17.4x	15.3x
EV/EBIT	21.9x	17.6x	20.7x	18.0x

This morning, Actelion has reported positive phase II data for the MERIT study which was investigating macitentan in CTEPH. This is obviously good news to help Opsumit exceed Tracleer's peak sales at some point although potential in this single indication is likely limited to USD100-200m, except if macitentan beats riociguat in phase III. But we are not sure that Actelion will take the risk of a head-to-head study against Bayer's drug. Conference call at 2pm today.

ANALYSIS

- CTEPH (Chronic thromboembolic PH, phase II) is usually defined as WHO Group 4 PH i.e. one among other forms of PH but not PAH. On top of high blood pressure in pulmonary arteries and low blood pressure in pulmonary capillaries, it is characterised by occlusive thrombi/emboli in the arteries. As such and unlike PAH, it is offered surgery as a therapeutic option (called pulmonary endarterectomy). Like PH in general, CTEPH is difficult to diagnose although it has often been associated with a history of acute pulmonary embolism that may somewhat help diagnosis. However, reports say that about 60% of CTEPH patients have not had any episode of acute PE. Echocardiogram, V/Q scan and MRA are often used to confirm diagnosis.
- Now, because PTE (pulmonary thromboendarterectomy) is potentially curative, it is the preferred treatment for patients with CTEPH. However, it is estimated that about one third at least are inoperable. For those, other options are required. In 2014, riociguat (Adempas), first-in-class soluble guanylate cyclase stimulator (sGC), has been made available by Bayer, achieved EUR182m in annual sales in 2015 and is growing 45% in 2016 (estimated EUR263m).
- In 2007 and 2008, the results of the phase III trial BENEFIT investigating bosentan in CTEPH were published at the ESC meeting and in the JACC. They were mixed as the drug showed benefits on PVR but no improvement in exercise capacity (6-minute walk test). One of the hypotheses formed to explain the failure of the drug to show superior efficacy was the too limited length of the trial (16 months).
- On top of being a different and potentially superior drug, macitentan has been included in a 24-week phase II trial called MERIT whose results are reported today. At this stage, Actelion has only considered inoperable patients (80 patients in MERIT) where Bayer studied riociguat both in inoperable and postoperative patients (about one third of patients who go surgery do not see their disease controlled). On average, riociguat showed a 39-meter improvement in the 6-minute walk test when recalculated (by the FDA) median difference vs placebo is considered, after 16 weeks. Actelion is reporting today a 34-meter difference for macitentan after 24 weeks (with only 1 meter in the placebo arm). As long as the effect on pulmonary vascular resistance (PVR), the reduction provided by macitentan after 16 weeks is statistically significant (-16%, p=0.04) but does not appear as high as it could have been hoped.

VALUATION

- The key question now is how well the data compares to what has been previously disclosed by Bayer with riociguat in this indication, bearing in mind once again that riociguat was investigated in both inoperable and post-operative CTEPH. A very first look at the numbers suggest it is not obvious. Therefore, it could be interesting to hear what Actelion's plans might be. We assume that a phase III trial will be initiated with macitentan in both inoperable and post-operative CTEPH patients. Using riociguat as a comparator could be risky however. Could macitentan be added to it? This afternoon's conference call is likely to tell us more about Actelion's strategy in this respect.

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