11th October 2016

Healthcare

Ipsen

Price EUR63.22

A full case vs a single sentence

Fair Value EUR67 (+6%) **BUY-Top Picks**

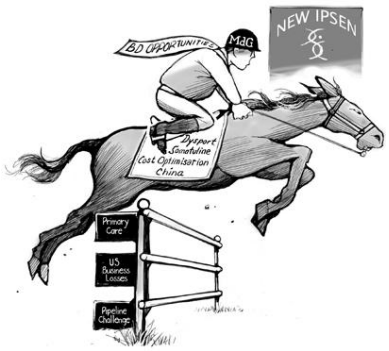
Bloomberg	IPN FP
Reuters	IPN.PA
12-month High / Low (EUR)	63.6 / 47.1
Market Cap (EUR)	5,264
Ev (BG Estimates) (EUR)	5,352
Avg. 6m daily volume (000)	75.50
3y EPS CAGR	13.8%

	1 M	3 M	6 M	31/12/15
Absolute perf.	8.3%	20.9%	21.3%	3.6%
Healthcare	-0.6%	-4.9%	0.6%	-9.5%
DJ Stoxx 600	-1.0%	4.5%	3.1%	-6.5%

YEnd Dec. (€m)	2015	2016e	2017e	2018e
Sales	1,444	1,566	1,714	1,866
% change		*8.5%*	*9.4%*	*8.9%*
EBITDA	366	407	462	544
EBIT	322.5	340.9	390.0	466.3
% change		*5.7%*	*14.4%*	*19.5%*
Net income	228.0	237.3	278.0	335.6
% change		*4.1%*	*17.2%*	*20.7%*

	2015	2016e	2017e	2018e
Operating margin	22.3	21.8	22.8	25.0
Net margin	12.5	14.0	14.1	15.9
ROE	15.5	16.9	16.7	17.8
ROCE	22.6	17.6	19.6	22.8
Gearing	-8.3	6.4	-0.2	-9.2

(€)	2015	2016e	2017e	2018e
EPS	2.78	2.89	3.39	4.09
% change	-	*4.1%*	*17.2%*	*20.7%*
P/E	22.7x	21.8x	18.6x	15.4x
FCF yield (%)	3.4%	3.7%	4.5%	5.5%
Dividends (€)	0.85	0.85	1.10	1.20
Div yield (%)	1.3%	1.3%	1.7%	1.9%
EV/Sales	3.6x	3.4x	3.1x	2.7x
EV/EBITDA	14.1x	13.2x	11.4x	9.4x
EV/EBIT	16.0x	15.7x	13.5x	10.9x



At ESMO principal investigator presented quite convincing phase II data for cabozantinib in 1L RCC that could be the base of a supplement filing … despite a more balanced view from discussant.

ANALYSIS

- What we are doing here is the summarized feedback from the third day at ESMO since CABOSUN phase II data were in highlight at the Presidential session.
- CABOSUN recruited 150 patients with clear-cell RCC naïve to therapy and having a poor or intermediate risk i.e. having the poorer prognosis (in 2L they will have between 5.4 and 16.6 months median survival rate), including 37% with bone metastases. This population represents between 70 and 75% of the overall RCC population.
- The primary endpoint was median PFS and it was expanded from 5.6 to 8.2 months (HR=0.69, p=0.012), with benefit across all subgroups, although it is fair to say that those with bone metastases benefited the most. The difference in ORR was also outstanding at 46% vs 18% (when assessed by investigator). Dose reductions occurred in 58% and 49% respectively in the cabo arm and the sunitinib arm and grade 3-4 side effects appeared very comparable across the two arms (65% vs 68%) and grade 5 AEs unfrequent (5% vs 4%). So these are very strong and consistent data in a setting where nothing has emerged since a long time.
- Everything was good until the last part of the presenter's speech when he stated that, based on the absence of median OS benefit (HR=0.80 with 30.3 months vs 21.8 but p=NS), he would not be comfortable prescribing the drug in 1L until confirmatory data from a phase III trial. This has come as a very unexpected comment from one of the most respected specialists in Europe. Exactly at that time, Exelixis's share price collapsed in the US.
- Asked similarly about what they would do, three US specialists invited by Ipsen and Exelixis went against this conclusion. They showed that sunitinib very much did as expected in this trial and like in previous ones and despite a limited follow-up, OS benefit is likely to be confirmed later. In any case, with a clear benefit on mPFS and ORR, cabozantinib proves superior to sunitinib and time will tell about nivolumab and others in this setting. In PC trials, it has been showed that cabozantinib might well prepare the milieu or make the environment permissive for a better effect of an IO drug. So cabo first makes a lot of sense, even though safety can be called into question. But patients might prefer an oral drug. Lastly, some preliminary phase I data, mostly in bladder cancers, showed interesting efficacy and safety data in heavily pre-treated patients that are reassuring for the safety of the combination and convinced Exelixis to start a phase II trial in bladder cancer. Cabo+Nivo vs Cabo then Nivo looks like an interesting phase III to perform.
- So, in the end, our belief is that cabozantinib, whatever its precise setting, is here to play a key role in RCC. Because of its mode of action that not only involves VEGFR pathway but also MET and AXL, it is now the TKi of choice and it is a bit too early to say how IO will navigate around. Moreover, 5-10% of patients that have immune diseases are not eligible to IO and those with bone mets are also clear candidates for cabo. So, the size of the market opportunity remains to be carefully measured but CABOSUN data are clearly helpful to give cabozantinib a central place in RCC.

VALUATION

- What can now happen with 1L RCC? Well, the optimism to be able to file on phase II data has clearly increased at Exelixis and Ipsen. The ability to file by the end of H1 2017 and to have a variation procedure in Europe making it possible to get an approval by year-end 2018 is real. This would be a major upside to our scenario and although the median duration of treatment based on mPFS might not be massively increased by getting in 1L, it is said that about 40% of patients are lost between 1L and 2L, thus reducing dramatically the target population.
- We will reassess our main asumptions at a later stage.

NEXT CATALYSTS

- 26 October 2016: Third-quarter sales - *Click here to download document*

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