

Sector View

Pharmaceuticals

	1 M	3 M	6 M	31/12/15
Healthcare	1.5%	9.6%	10.2%	-4.0%
DJ Stoxx 600	5.3%	2.6%	4.7%	-6.7%

*Stoxx Sector Indices

Companies covered

Company	Rating	Price
ACTELION	NEUTRAL	CHF180
Last Price	CHF165,3	Market Cap. CHF17,813m
ASTRAZENECA	BUY	5400p
Last Price	5220p	Market Cap. GBP66,022m
BAYER	NEUTRAL	U.R.
Last Price	EUR95,87	Market Cap. EUR79,280m
GLAXOSMITHKLINE	BUY	1810p
Last Price	1694,5p	Market Cap. GBP82,603m
IPSEN	BUY	EUR66
Last Price	EUR60,67	Market Cap. EUR5,056m
NOVARTIS	NEUTRAL	CHF87
Last Price	CHF81,55	Market Cap. CHF214,241m
NOVO NORDISK	NEUTRAL	DKK385
Last Price	DKK330	Market Cap. DKK664,146m
ROCHE HOLDING	BUY	CHF293
Last Price	CHF250,3	Market Cap. CHF175,852m
SANOFI	NEUTRAL	EUR83
Last Price	EUR72,53	Market Cap. EUR93,484m
SHIRE PLC	BUY	6900p
Last Price	5145p	Market Cap. GBP46,315m
UCB	NEUTRAL	EUR80
Last Price	EUR69,48	Market Cap. EUR13,514m

Opdivo fails in 1L NSCLC in monotherapy

BMS announced last Friday that CheckMate-026 had failed to reach its primary endpoint, meaning that Opdivo monotherapy failed to show superiority on PFS vs chemotherapy in previously untreated patients with PD-L1 positive NSCLC. This is the first major failure for Opdivo and the surprise comes mainly from the selection of patients. It gives even more credit to those who believe that the future of immune-oncology is mainly in combinations. And so this is good news for Roche and even more so for AstraZeneca because the big 1L NSCLC market may be first addressed by them rather than by US peers. They should respectively report phase III data from IMpower150 and MYSTIC respectively next year. To a lesser extent, the news is also positive for Ablynx and Innate.

ANALYSIS

- CheckMate-026 was supposed to recruit about 535 patients with previously untreated NSCLC cancer with PD-L1 positive status that were randomised in two arms to receive either chemotherapy (gemcitabine or CarboTax for squamous forms, Carbo/Cis-Alimta for non-squamous forms) or Opdivo. The trial failed to reach its primary endpoint and to demonstrate superior PFS compared to CT. This is all the more surprising in that back in June, Keytruda succeeded in a fairly similar study named KEYNOTE-024 where both PFS and OS endpoints were met. It is fair to say that only non-squamous NSCLC patients were eligible and that the PD-L1 degree of overexpression was different (>50% in Merck's trial, >5% in BMS's trial). If positive, BMS would have opened a much larger market opportunity for Opdivo than Merck did with Keytruda.
- So, what does this tell us? Well, probably that monotherapy with an IO agent has limitations at some point in addressing all tumour types in all settings. Referring to page 9 of our Oncology Report published in July after our Oncology Day at Curie (link [here](#)), we said that combining IO agents was the best way to address tumour heterogeneity and complexity.
- Clearly, this failure is good news for Roche and AstraZeneca because they are strong believers in combinations as synergies can be developed by targeting several pathways simultaneously. With CheckMate-026 positive, all combinations in development would have been compelled to show clearly how much extra benefit they were offering above and beyond Opdivo. Although all trials include PD-L1 monotherapy arms, this would have made the objective more difficult to reach, from a regulatory standpoint first and then from a price perspective too. Because Keytruda was successful only in PD-L1 high expressers, the bar is not so high yet.
- So now Roche and AstraZeneca are next to deliver. Very early in 2017, Roche is expected to provide data with IMpower150, which compares Tecentriq/CT to CT +/- Avastin while AstraZeneca should come shortly afterwards with the highly awaited MYSTIC trial which should be the first CT-free combination (durva/treme) in a similar setting. Positive results would give the two companies a significant advantage over peers in this top prioritized 1L NSCLC market segment that is worth several billions (all the more so if IO/IO proves standard). CheckMate-227 (Opdivo/Yervoy) is only expected to deliver results in early 2018 (KEYNOTE-189 should report in September 2017).
- So, to summarise, Roche and AstraZeneca still have to deliver positive results with their own compounds but the failure of CheckMate-026 gives more credit to combination strategies.
- To a lesser extent, we think the news is also positive for Ablynx and Innate Pharma as they are respectively involved in partnerships with Merck & Co and BMS to combine some of their drugs with their PD-1 checkpoint inhibitors. Note also that 1/ last year, MSD expanded its I-O partnership with ABLX, which now includes up to 17 targets for a total deal value of up to USD5.7bn (INDS expected in late 16/early 17); 2/ we expect some Phase Ib data (including PFS?) involving lirilumab/nivolumab in "inflamed" solid tumours at the upcoming ESMO congress.

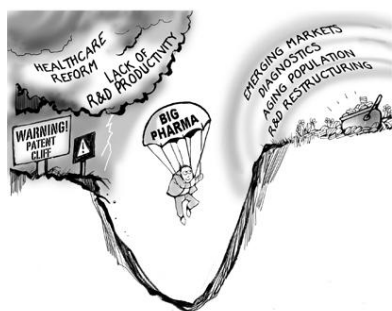
VALUATION

- We are making no change to any of our numbers.

NEXT CATALYSTS

- 7-11th October 2016: ESMO congress in Copenhagen

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SELL ratings 10,7%

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