6th June 2016

Sector View

Pharmaceuticals

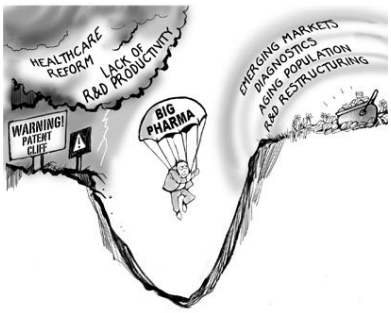
First feedback from ASCO 2016: confirmations

	1 M	3 M	6 M	31/12/15
Healthcare	4.9%	5.0%	-5.9%	-6.7%
DJ Stoxx 600	1.7%	0.6%	-8.3%	-6.7%

*Stoxx Sector Indices

Companies covered

ACTELION		**BUY**	**CHF173**
Last Price	CHF165	*Market Cap.*	CHF18,831m
ASTRAZENECA		**BUY**	**5100p**
Last Price	4039p	*Market Cap.*	*GBP51,076m*
BAYER		**NEUTRAL**	**U.R.**
Last Price	EUR89,34	*Market Cap.*	*EUR73,880m*
GLAXOSMITHKLINE		**BUY**	**1700p**
Last Price	1459p	*Market Cap.*	*GBP71,080m*
IPSEN		**BUY**	**EUR63**
Last Price	EUR56,52	*Market Cap.*	*EUR4,705m*
NOVARTIS		**NEUTRAL**	**CHF89**
Last Price	CHF79	*Market Cap.*	*CHF207,542m*
NOVO NORDISK		**NEUTRAL**	**DKK400**
Last Price	DKK370,7	*Market Cap.*	*DKK746,057m*
ROCHE HOLDING		**BUY**	**CHF293**
Last Price	CHF258,2	*Market Cap.*	*CHF181,402m*
SANOFI		**NEUTRAL**	**EUR83**
Last Price	EUR72,49	*Market Cap.*	*EUR93,283m*
SHIRE PLC		**BUY**	**6500p**
Last Price	4407p	*Market Cap.*	*GBP39,600m*
UCB		**NEUTRAL**	**EUR80**
Last Price	EUR66,78	*Market Cap.*	*EUR12,989m*



During the first few days of the ASCO 2016 meeting currently taking place in Chicago, we have mainly seen confirmations of several drug classes, rather than pure discoveries. Among them, of course, the PD-1/PD-L1 class is making further inroads in several solid tumours including subgroups of lung cancer or bladder cancer but also in colorectal cancer, the CDK 4/6 class in breast cancer, first promising data for OX40 in combination with PD-L1 on safety and positive results also for cabozantinib in RCC, daratumumab in MM and for ramucirumab in combination with pembro. In the end however, it is hard to extract a winner from these first three days.

ANALYSIS

- For Exelixis and **Ipsen** that unveiled full data from the METEOR phase III study assessing the value of cabozantinib in advanced line RCC, ASCO is positive in that it offered a scene to detail the recently-disclosed clinical data included in the P.I. leaflet of Cabometyx when approved by the FDA mast month. Median PFS was 7.4 months vs 3.8 months with cabozantinib vs everolimus (HR=0.58) and median duration of treatment 8.3 months vs 4.4 months. Even more importantly, median OS was 21.4 months vs 16.5 months (HR=0.66) and the benefits were seen across the subgroups, including in presence of bone metastases and irrespectively of the previously used therapy in first-line. This data is highly supportive of the use of Cabometyx in second-line RCC although it is fair to say also that BMS presented equally solid data for Opdivo in the same indication. PD-1/PD-L1 drugs are increasingly seen as very effective over the long-term and data represented by BMS was supportive of tthistheory since 4-year and 5-year data of phase II and phase I study follow-ups show high survival rates compared to history in RCC. 5-year survival rates for patients with advanced RCC are usually somewhere between 10 and 15%. 4-year and 5-year survival rates with Opdivo were respectively 38% and 34%. It is highly likely that both Opdivo and Cabometyx will show survival benefit in first and second line in RCC and take the lead in that market over the next few years. Cabometyx is a significant opportunity for Ipsen which is expecting European approval for the drug in September and is preparing for launch early in 2017. Our understanding is that Ipsen has already recruited top managers for its new oncology franchise.

- **AstraZeneca** presented two interesting clinical data results over the week-end. The first relates to olaparib and confirms its high value for platinum-sensitive ovarian cancer where the drug is already approved. A third interim analysis has established a 27% reduction in the risk of death in the overall population and a 38% reduction in women whose cancer has BRCA1/2 mutations. Lynparza now has to climb from third into second and first-line of BRCA1/2 mutated ovarian cancer and to prove efficacy in breast and prostate cancers. Studies are ongoing. The other result concerns durvalumab in urothetial bladder cancer where data can be considered solid in comparison with what Roche historically disclosed with atezolizumab. ORR is 31% in all-comers and 46% in patients with PD-L1 high-expressing tumours. The disease control rate was 48% and 57% respectively. Roche disclosed updated data for its IMvigor210 phase II trial with Tecentriq, recently approved in this indication, with 24% ORR and 14.8 months median OS. AZN's durvalumab is currently evaluated in an ongoing phase III trial called DANUBE where it is also combined with tremelimumab.

- **Genmab**: Details from the CASTOR study (which evaluated daratumumab in combination with bortezomib and dexamethasone) in multiple myeloma were presented yesterday. Efficacy-wise, we'd notably underline the following points: 1/ the response rates obtained with dara/bort/dex (Dbd) were a bit higher than what we saw with Amgen's Kyprolis, but the differences in PFS are much more significant… confirming our view that immune-oncology agents tend to be much more potent when we look at endpoints like PFS or OS; 2/ the 1-year PFS rate stood at 60.7% within the active arm vs 26.9% for the control arm (bort/dex)… hence a Hazard Ratio (HR) of 0.39; 3/ should we limit our analysis to second-line patients (R/R to one prior therapy), the 1-year PFS rate and the HR was was impressively much better (77.5% vs 29.4%, HR: 0.31, p<0.0001).

  Obviously, this data is more than encouraging and we expect it has gone down well with the street and the scientific community… We also believe 1/ the upcoming presentation of POLLUX at the EHA meeting (12th June 2016) should add some more positive momentum; 2/ along with CASTOR, it will ensure a fairly fast adoption among second-line patients.

- For **Roche,** beyond what we already commented on, some updated data on the combination of atezolizumab with Abraxane in triple negative breast cancer in phase Ib is worth pointing out, bearing in mind that a phase III is ongoing (350 patients, First-line, FPI: June 2015, estimated completion: 2019, Endpoint: PFS). In the phase Ib, patients could have been treated with up to three prior lines of therapy. DCR was over 80% and relatively consistent across the different lines of treatment.

  It also presented updated data of its POPLAR phase II trial that compares Tecentriq with chemo in NSCLC and results are even stronger than previous ones as median OS moved from 11.4 months to 12.6 months (HR=0.69) and mDOR from 14.3 to 18.6 months (HR=0.32). That said, they are very similar to the same results included in Opdivo's prescribing information i.e. mOS of 12.2m vs 9.4m for docetaxel (same comparator as in POPLAR where they are 12.6m vs 9.7m respectively) with a mDOR of 17 months. Note here that Merck disclosed data showing that combining Keytruda with chemotherapy in first-line NSCLC resulted in ORR ranging from 48 to 71% with best combination with carboplatin and pemetrexed vs CarboTax or CarboTax/Avastin, raising the bar fairly high.

  AbbVie provided some more data involving Venclexta (venetolax), its oral BCL2 inhibitor co-developed with Roche, in multiple myeloma and as part of a combination regimen with bortezomib and dexamethasone. The overall response rate was superior to 80% in patients who received between one and three prior therapies; but more precisely we'd note that 1/ the ORR stood at 100%, of which 84% were at least very good partial responses, in bortezomib-naïve ones; and 2/ it reached 71% in bortezomib-sensitive patients. In our view, such preliminary data are quite competitive compared to Kyprolis (carfilzomib)… So adding this to the fact that Venclexta is much more convenient (oral vs IV), we believe it may grab some shares from Amgen's compound at some point.

- Lastly, nothing really new about CDK4/6 inhibitors but this confirms that the battle between Pfizer, (first-in-class with Ibrance), Novartis (as a fast-follower with LEE011 that recently stopped a trial early based on good interim efficacy data) and Lilly (slightly behind that has just presented the results of the phase II trial MONARCH 1 ORR=19.7%, mPFS=6m, CDR=42.4%) is likely to be fierce. Two phase III trials are ongoing in combination with fulvestrant and vs aromatase inhibitor.

VALUATION

- No unexpected data was presented over the weekend that could impact FVs of any of the stocks we cover.
- Despite expected strong competition from PD1-PD-L1 and Opdivo in particular, we see upside to our Cabometyx numbers. Very good long-term OS data for Opdivo bodes well for use in first-line and so we see the opportunity for Cabo in second-line as intact. Further upside might come from use in combination of the two drugs, provided toxicity is acceptable.

NEXT CATALYSTS

- Today and tomorrow: last two days of the ASCO 2016 meeting

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