



10th October 2016

## BG's Wake Up Call

	Last close	Daily chg (%)	Chg YTD (%)
<b>Indices</b>			
Dow Jones	18240.49	-0.15%	+4.68%
S&P 500	2153.74	-0.33%	+5.37%
Nasdaq	5292.4	-0.27%	+5.69%
Nikkei	16860.09	-0.23%	-11.42%
Stoxx 600	339.641	-0.93%	-7.16%
CAC 40	4449.91	-0.67%	-4.04%
<b>Oil /Gold</b>			
Crude WTI	49.81	-1.25%	+33.90%
Gold (once)	1253.36	+0.15%	+17.98%
<b>Currencies/Rates</b>			
EUR/USD	1.11765	+0.07%	+2.89%
EUR/CHF	1.09475	+0.02%	+0.68%
German 10 years	-0.049	-35.95%	-107.69%
French 10 years	0.253	+4.83%	-74.24%
Euribor	-0.304	0.00	+132.06%

### Economic releases :

Date	
10th-Oct	10h30 EUZ - Sentix Investor Confidence Oct. (6 E) US - Banks Closed Markets Open

### Upcoming BG events :

Date	
21st-Oct	KORIAN (BG Geneva roadshow with CFO)
28th-Oct	IMERYS (Paris roadshow)
8th-Nov	LVMH (BG Luxembourg roadshow with IR)
14th-Nov/ 15th-Nov	4th Paris Healthcare Conference
18th-Nov	ENGIE (BG Luxembourg roadshow with IR)
24th-Nov	IMERYS (BG London roadshow with IR)

### Recent reports :

Date	
7th-Oct	ALTICE Lower risk profile
7th-Oct	SAINT GOBAIN : Endless sluggishness is not our scenario (report released today)
4th-Oct	CASINO We are cautious ahead of Q3 figures
4th-Oct	LAFARGE HOLCIM This is still a Buy
15th-Sept	Remy Cointreau : It keeps getting better
14th-Sept	Automotive Innovation: the only way to stand out!

List of our Reco & Fair Value : Please click here to download



### ASTRAZENECA

**BUY, Fair Value 5220p (+3%)**

#### One year to go before kick-off

The breakfast we held last Friday with the group's CEO and CFO in Paris was very insightful and much appreciated by attendees. In spite of a few hiccups on the way, management is developing its strategy nicely and the level of confidence in achieving long-term targets is high. Key assets are due in respiratory and nephrology but the most exciting franchise is still oncology where the group is not ruling out the prospect of generating as much as 40% of its revenues by 2023.

### LUXOTTICA

**NEUTRAL, Fair Value EUR52 vs. EUR54 (+27%)**

#### Q3 2016 sales preview: a more harmful impact from the MAP policy

The Retail division could post more favourable trends (Sunglass Hut US, first store openings, etc.) but these first improvements will be overshadowed by the group's well-known own initiatives in Wholesale (MAP policy at Ray-Ban US and direct go-to-market approach in mainland China). Following our revised forecast for Q3 (+1.1%e adj. FX-n), our FY assumption (+1.8%e) is now slightly more cautious than FY guidance (+2-3%), but still implies 3% growth in Q4. Our revised FY forecast leads to a new FV of EUR52 vs. EUR54.

### HEALTHCARE

#### Feedback from ESMO – Part 1

At the end of the first few days of congress in Copenhagen, we would say that CDK4-6 were very much endorsed as new likely SoC in ER+ BC (which is good for Novartis, despite a position of challenger behind Pfizer), whereas the jury is still out in NSCLC about the size of the opportunity although Roche did the job with OAK (in 2L/3L). 1L is still very much open.

### WORLDLINE

#### We consider the current share price as a good entry point

After losing 9% since its peak on 2nd September, we believe the current price is attractive enough to play positive momentum and more visibility in a couple of days. This should begin with the Q3 release on 19th October (the group should give FY guidance including the Equens/Paysquare and KB deals, in order for the consensus to officially integrate them into its model), and Atos' capital market day on 8th November). At 9.7x EV/EBITDA over 12 rolling months, we advise investors to target 12x. Then, in the coming months, the group has the means to sign a new acquisition to give even more upside to this multiple. We maintain our Buy recommendation and FV of EUR31.

### In brief...

**GENMAB, Priority review obtained... Now expecting a label expansion in Q1 2017**

**INNATE PHARMA, Let's wait for the SITC to get a view of the efficacy profile of liri/nivo**

**NICOX, AC-170 got a CRL... We see the glass as half full**

**NOVO NORDISK, Unexpected delay for ultra-fast acting insulin in the US**

**LAFARGEHOLCIM, Another step in the divestment process**

Healthcare

**AstraZeneca**

Price 5,086p

One year to go before kick-off

Fair Value 5220p (+3%)

BUY

Bloomberg	AZN LN
Reuters	AZN.L
12-month High / Low (p)	5,220 / 3,774
Market Cap (GBP)	64,339
Ev (BG Estimates) (GBP)	76,580
Avg. 6m daily volume (000)	2,712
3y EPS CAGR	-3.6%

The breakfast we held last Friday with the group's CEO and CFO in Paris was very insightful and much appreciated by attendees. In spite of a few hiccups on the way, management is developing its strategy nicely and the level of confidence in achieving long-term targets is high. Key assets are due in respiratory and nephrology but the most exciting franchise is still oncology where the group is not ruling out the prospect of generating as much as 40% of its revenues by 2023.

ANALYSIS

- Well advanced into the journey now – Pascal Soriot started as a CEO at AstraZeneca on 1st October 2012 and it was interesting to hear where we now stand. He actually divides the journey into three periods: 2012-2015 where the portfolio had to be rebuilt; 2016-2017 which is the trickiest period as this is when the patent cliff hits the bottom; 2018 and beyond when the company is poised to deliver very high growth rates.
- Very transparently, Pascal Soriot acknowledged that LT targets would probably differ in nature compared to initial expectations. Out of a very focused portfolio, Cardio/Metabolism is likely to be smaller than anticipated whereas oncology will be bigger. How much bigger? Depending on the outcomes of ongoing trials, this will be somewhere between 30% and 40% of total revenues in 2023. So far, we expect Oncology to represent 30% of total sales in 2022. Assuming that we are not too optimistic about non-Oncology assets, where might the difference come from? At least three potential pockets: (i) Tagrisso, which should benefit from both an expanded target market (data in 1L and on brain metastases to come) and limited competition as many have either failed or moved away. Soriot suggested that Tagrisso could now be “well in excess of USD3bn” with an “Herceptin-like type of profitability”. Clearly, we have to re-assess the case here as we have only USD1.6bn in our model; (ii) there are a wide range of scenarios for durvalumab but our current PoS of 50% only translates into USD1.875m sales in 2022 which leaves much more upside than downside at first glance, whatever happens to MYSTIC we would say. In any case, MYSTIC is not going to be black or white and a complete failure is highly unlikely; (iii) although it is at an earlier stage, there is also excitement around AZD1775, the WEE-1 inhibitor, notably in combination with Lynparza. We have no sales for this one, which is currently in phase II, in our model.
- In Cardio/Metabolism, despite disappointments for Diabetes in the US and with Brilinta (note that he mentioned that SOCRATES was actually not totally negative but likely to short in duration whereas EUCLID was only 40-45% PoS in their LT plans), they are very optimistic about their renal franchise and are expecting (i) ZS-9 to be approved early in 2017 in the US and to show it is a great drug that is well designed to tap a significant market; (ii) roxadustat to deliver first results in China in 2017 and to pave the way for success in a pre-dialysis setting; (iii) all this to leverage an existing Diabetes franchise which is very strong, especially outside the US.
- The last two growth drivers Pascal Soriot spent some time on were: (i) benralizumab, which is clearly AZN's best chance to keep its Respiratory franchise in growth mode as Symbicort (also because of Advair's analogues) is likely to decline. His guess is that benralizumab should show similar results to GSK's Nucala on exacerbations but superior profile on FEV1 whereas the drug is more convenient for the patient (no reconstitution, every other month). And so he believes benra could be an Humira-like product in the class; (ii) China is another growth opportunity for the group in which it has invested heavily (the sales force has been doubled over the last 3-4 years) to achieve leadership position (number 1 or 2 head and neck with Pfizer). Several drugs have still to be launched there including Farxiga or Brilinta, with very high hopes.

VALUATION

- Pascal Soriot and Marc Dunoyer strongly impressed a crowded room of investors. The path forward is very clear. Now of course, 2017 will be another (but the last) tough year to go through. And the share's performance in 2017 will be highly dependent on a few outcomes, including MYSTIC for sure. We will reassess the case and our numbers shortly.

NEXT CATALYSTS

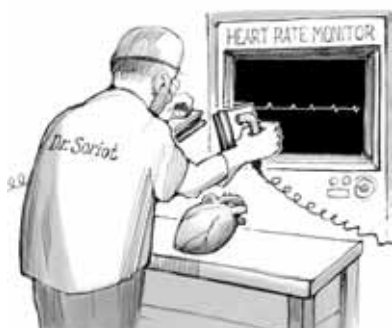
- 8-12th October 2016: ESMO meeting (Copenhagen) - [Click here to download](#)

	1 M	3 M	6 M	31/12/15
Absolute perf.	4.3%	10.7%	22.0%	10.2%
Healthcare	-2.8%	-5.0%	0.1%	-10.0%
DJ Stoxx 600	-3.1%	5.4%	3.5%	-7.2%

YEnd Dec. (USDm)	2015	2016e	2017e	2018e
Sales	23,641	21,600	20,309	21,166
% change		-8.6%	-6.0%	4.2%
EBITDA	5,937	4,177	6,039	6,286
EBIT	4,114	3,150	5,386	5,214
% change		-23.4%	71.0%	-3.2%
Net income	5,390	5,031	4,965	4,835
% change		-6.7%	-1.3%	-2.6%

	2015	2016e	2017e	2018e
Operating margin	17.4	14.6	26.5	24.6
Net margin	6.8	1.0	9.3	10.1
ROE	8.6	1.4	13.4	16.8
ROCE	16.2	14.5	12.4	11.9
Gearing	47.7	100.3	128.5	163.5

(USD)	2015	2016e	2017e	2018e
EPS	4.26	3.98	3.93	3.82
% change	-	-6.7%	-1.3%	-2.6%
P/E	14.9x	15.9x	16.1x	16.6x
FCF yield (%)	NM	NM	2.5%	2.3%
Dividends (USD)	2.80	2.80	2.80	2.80
Div yield (%)	4.4%	4.4%	4.4%	4.4%
EV/Sales	3.8x	4.4x	4.8x	4.7x
EV/EBITDA	15.0x	22.8x	16.2x	15.9x
EV/EBIT	21.6x	30.3x	18.1x	19.2x



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Luxury & Consumer Goods

**Luxottica**

Price EUR40.85

Q3 2016 sales preview: a more harmful impact from the MAP policy

Fair Value EUR52 vs. EUR54 (+27%)

NEUTRAL

Bloomberg	LUX.IM
Reuters	LUX.MI
12-month High / Low (EUR)	65.6 / 40.9
Market Cap (EURm)	19,775
Ev (BG Estimates) (EURm)	20,539
Avg. 6m daily volume (000)	865.7
3y EPS CAGR	8.0%

The Retail division could post more favourable trends (Sunglass Hut US, first store openings, etc.) but these first improvements will be overshadowed by the group's well-known own initiatives in Wholesale (MAP policy at Ray-Ban US and direct go-to-market approach in mainland China). Following our revised forecast for Q3 (+1.1%e adj. FX-n), our FY assumption (+1.8%e) is now slightly more cautious than FY guidance (+2-3%), but still implies 3% growth in Q4. Our revised FY forecast leads to a new FV of EUR52 vs. EUR54.

ANALYSIS

- MAP policy at Ray-Ban North America: a higher headwind in Q3.** In Q2 Ray-Ban's US sun business fell by ~5%e mainly due to the implementation of the "Minimum Advertised Price" policy, which had a direct impact on online sales (-50% in Q2). As highlighted in our previous comments, the group could not communicate on a precise tipping point in the ST. Hence our estimates retained the same negative impact until the anniversary effect in Q2 201,7 but it now appears that this headwind could be higher-than-expected in Q3 given its implementation in July. This situation confirms that this MAP policy, although necessary to protect brand equity, remains the main drag on the group's organic growth.

- Mainland China affected by the change in distribution model.** Indeed, the group is adopting a direct go-to-market approach for its Wholesale business, i.e. shifting from independent distributors to own distribution, causing sales disruptions in the ST, while the Chinese sunglass market remains robust despite a more challenging macro environment. Note that LUX's Head of Wholesale and Retail for Greater China Paolo Ciarlariello recently left the group and this departure might be explained by these reorganisations.

- First signs of improvement in Retail.** The division started enjoying some levers in Q3: (i) more favourable weather conditions that should be particularly positive for Sunglass Hut US, (ii) the first store openings of LensCrafters @ Macy's and Target Optical across the US (+80 and +40 stores to be opened throughout H2) and (iii) the US calendar realignment that would contribute positively in H2 (+1 day in Q3 and +3 days in Q4).

- We nudge down our FY16 assumptions by 60bp.** This is the direct consequence of more cautious expectations for Q3, particularly in the Wholesale Division given a more adverse impact from the MAP policy and a complicated sport sunglass channel (Oakley). The three above-mentioned drivers for Retail are reflected in the gradual acceleration, notably a higher contribution from the store openings and the retail calendar realignment. Consequently, our FY FX-n growth for 2016 (+1.8%e vs. 2.4%e previously) is now below the Group's FY guidance of 2-3%, which is justified given low visibility, particularly with regards to the MAP policy.

Adj. FX-n by division:

%	Q1 16	Q2 16	Q3 16e	Q4 16e	2016e
Wholesale	2.1	0.2	-2.0	0.5	0.3
Retail	1.6	2.3	3.0	4.5	2.8
<b>Total Luxottica</b>	<b>1.8</b>	<b>1.4</b>	<b>1.1</b>	<b>3.0</b>	<b>1.8</b>

Source: Company Data, BG ests

VALUATION

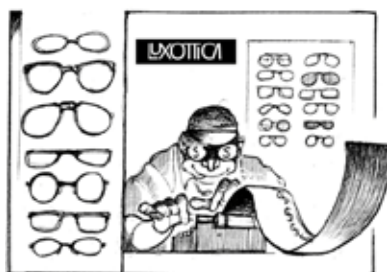
- Initially we were hoping for a slight acceleration in Q3, mainly driven by the first store openings and more favourable weather conditions whilst the MAP policy headwind was expected to be in line with Q2. The latter would eventually be a higher drag than the group's expectations (and our forecasts), leading to this another weak organic growth. Hence our new FV of EUR52 vs. EUR54 is a consequence of our new FY assumptions.

- We still believe that the group's initiatives, though painful in the ST, should enable LUX to restore traction in the MT, especially since the global optical market continues to grow. At 13x 2017e EV/EBIT, the stock is trading at a 20% discount vs. 2004-16 historical average.

NEXT CATALYSTS

- Luxottica will release Q3 2016 sales on 24th October.

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Sector View

Healthcare

Feedback from ESMO – Part 1

	1 M	3 M	6 M	31/12/15
Healthcare	-2.8%	-5.0%	0.1%	-10.0%
DJ Stoxx 600	-3.1%	5.4%	3.5%	-7.2%

\*Stoxx Sector Indices

Companies covered

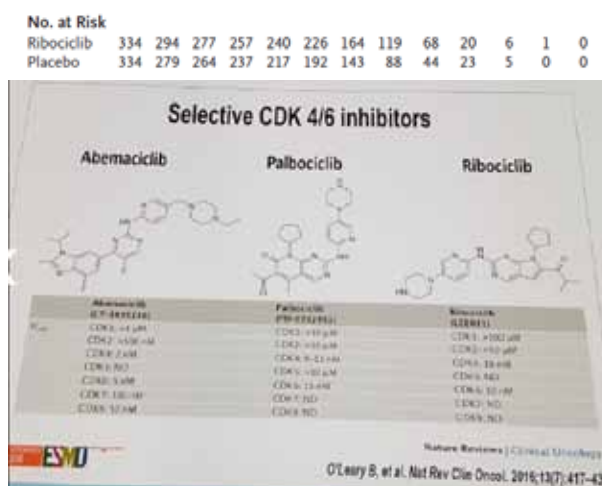
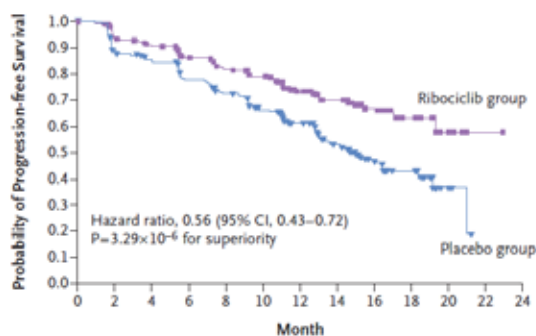
Company	Recommendation	Price	Market Cap
ABLYNX	BUY	EUR18	
Last Price		EUR10.92	Market Cap. EUR665m
ACTELION	NEUTRAL	CHF180	
Last Price		CHF167.3	Market Cap. CHF18,028m
ADOCIA	BUY	EUR90	
Last Price		EUR51.99	Market Cap. EUR356m
ASTRAZENECA	BUY	5220p	
Last Price		5086p	Market Cap. GBP64,339m
BAYER	NEUTRAL	EUR98	
Last Price		EUR89.8	Market Cap. EUR74,260m
BIOMERIEUX	NEUTRAL	EUR130	
Last Price		EUR132.55	Market Cap. EUR5,230m
BONE THERAPEUTICS	BUY	EUR30	
Last Price		EUR10.54	Market Cap. EUR72m
CELLECTIS	BUY	EUR37	
Last Price		EUR20.28	Market Cap. EUR717m
CELYAD	NEUTRAL	EUR21	
Last Price		EUR19.26	Market Cap. EUR179m
DBV TECHNOLOGIES	BUY	EUR91	
Last Price		EUR67.5	Market Cap. EUR1,627m
ERYTECH	BUY	EUR47	
Last Price		EUR17.5	Market Cap. EUR139m
FRESENIUS MED.CARE	BUY	EUR94	
Last Price		EUR74.4	Market Cap. EUR22,851m
FRESENIUS SE	BUY	EUR78	
Last Price		EUR69.53	Market Cap. EUR38,028m
GALAPAGOS	BUY	EUR64	
Last Price		EUR57.73	Market Cap. EUR2,665m
GENEURO	BUY	EUR18.2	
Last Price		EUR7.05	Market Cap. EUR103m
GENMAB	BUY	DKK1600	
Last Price		DKK1136	Market Cap. DKK68,443m
GLAXOSMITHKLINE	BUY	1810p	
Last Price		1709p	Market Cap. GBP83,327m
INNATE PHARMA	BUY	EUR18	
Last Price		EUR11.01	Market Cap. EUR594m
IPSEN	BUY	EUR67	
Last Price		EUR62.98	Market Cap. EUR5,244m
KORIAN	NEUTRAL	EUR28	
Last Price		EUR27.87	Market Cap. EUR2,235m
MORPHOSYS	BUY	EUR64	
Last Price		EUR43.32	Market Cap. EUR1,150m
NOVARTIS	NEUTRAL	CHF87	
Last Price		CHF76.55	Market Cap. CHF201,106m
NOVO NORDISK	NEUTRAL	DKK355 vs 360	
Last Price		DKK270.3	Market Cap. DKK543,996m
ORPEA	BUY	EUR85	
Last Price		EUR76.51	Market Cap. EUR4,595m
QIAGEN	BUY	EUR26	
Last Price		EUR24.435	Market Cap. EUR5,857m

At the end of the first few days of congress in Copenhagen, we would say that CDK4-6 were very much endorsed as new likely SoC in ER+ BC (which is good for Novartis, despite a position of challenger behind Pfizer), whereas the jury is still out in NSCLC about the size of the opportunity although Roche did the job with OAK (in 2L/3L). 1L is still very much open.

Highlights from day 1

If we had to take home with only one major idea from day 1, it would be the growing evidence of the strong influence of CDK4-6 inhibitors in ER-positive breast cancer. Be it in a presentation about biomarker analysis in the PALOMA-2 study comparing palbociclib/letrozole to letrozole or in the big presentation during the Presidential Symposium of the MONALEESA-2 phase III results, the common conclusion is that CDK4-6 inhibitors work irrespectively of the subgroups. Different hypothesis have been tested, including p16 or Ki-67 status are predictive markers, but it failed to establish a difference. Finally, as he concluded that CDK4-6 inhibitors would probably be game-changing for the treatment of ER+ BC, invited discussant S. Johnston simply concluded by asking how these drugs should be used. And maybe the only relevant question left at this stage is to know if endocrine sensitivity vs endocrine naïve vs endocrine resistant tumors makes a difference or if they deserve being used across the board. But true is that the results are impressive when this compares to aromatase inhibitors that had already been a significant advance in the treatment of ER+ BC. Median PFS jumped from 14.5 to 24.8 months in the PALOMA-2 study whereas it is not yet reached in MONALEESA-2 by the active arm vs 14.7 months for the comparative arm (HR=0.556).

Fig.1: PFS results in MONALEESA-2 phase III trial (left) – Comparison of CDK4-6 inhibitors (right)



Source : NEJM(left), picture from ESMO 2016 (right)

In both cases, it has been highlighted how quickly the two curves were separating (especially in contrast with fulvestrant that presented also solid data in FALCON but with late benefit, almost exclusively when there is no visceral disease). And safety is globally very good with limited numbers of grade 3 side-effects (mostly neutropenias and leukopenias, including 5 cases of febrile neutropenias), that are asymptomatic and usually manageable with treatment interruption. We would note however that there were 4 patients that met criteria of Hy's Law in combination arm. As a second-to-market agent, this is something regulators might pay more attention to. That said, presenters mainly commented the results as meaningful confirmatory results of palbociclib, now forming the evidence of the central role to be played by CDK4-6 inhibitors in 1L ER+ breast cancer. Pfizer's drug is likely to take the lion's share of this market (all the more so if it succeeds in the adjuvant setting too) but LEE011 will nevertheless be a multi-blockbuster drug even with a 20% share (or more).

## BG's Wake Up Call

Company	Recommendation	Price	Market Cap
ROCHE HOLDING	BUY	CHF293	
Last Price	CHF238.3	Market Cap.	CHF167,421m
SANOFI	NEUTRAL	EUR83	
Last Price	EUR68.8	Market Cap.	EUR88,686m
SHIRE PLC	BUY	6900p	
Last Price	5196p	Market Cap.	GBP46,918m
UCB	NEUTRAL	EUR80	
Last Price	EUR67.74	Market Cap.	EUR13,176m
ZEALAND	BUY	DKK172	
Last Price	DKK104.5	Market Cap.	DKK2,723m

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Beyond CDK4-6 inhibitors, another new class was under the spotlights: PARP inhibitors. However, our guess is that it will be much more the case next year as much more evidence will be available to assess their value in ovarian and in breast cancer. This is all the more true that olaparib was unfortunately in the focus for a trial called GOLD where it failed to reach the pre-specified primary endpoint and the conclusion is that the issue is the reflection of a mistake in the design of the study. There is a strong correlation in the literature between ATM cell status or p53 function and PARP inhibition. Although it was clearly confirmed in phase II where olaparib came out with very encouraging data, the phase III GOLD only included 18% of patients with ATM-negative tumors (vs 50% in phase II), translating into an overall benefit of 1.9 months in terms of median OS with a p-value of 0.0262 when 0.025 was required for statistical significance. The dose and the CT (paclitaxel vs irinotecan) used were also questioned.

In contrast with GOLD, the strong NOVA study results were also presented that were investigating Tesaro's PARP inhibitor in maintenance therapy for recurrent ovarian cancer and they were simply outstanding irrespectively of the subgroups i.e. with or without BRCA mutation although it is fair to say that in non-gBRCA mutated patients, the efficacy was driven by HRD-positive patients. In gBRCA and non-gBRCA but with HRD+, median PFS was 3-4 fold higher than placebo. Importantly though, it looks like the more intense the prior platinum-based therapy the better the results, confirming that platinum response correlates to response to PARP inhibitors. This might question the use of PARP inhibitors in naive patients (where combinations may be envisaged, like with WEE-1 inhibitors at AstraZeneca). There will be much more data to share on PARP inhibitors in 2017, including in breast cancer.

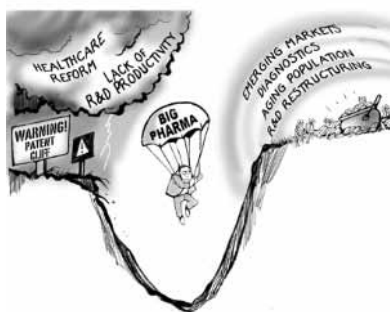
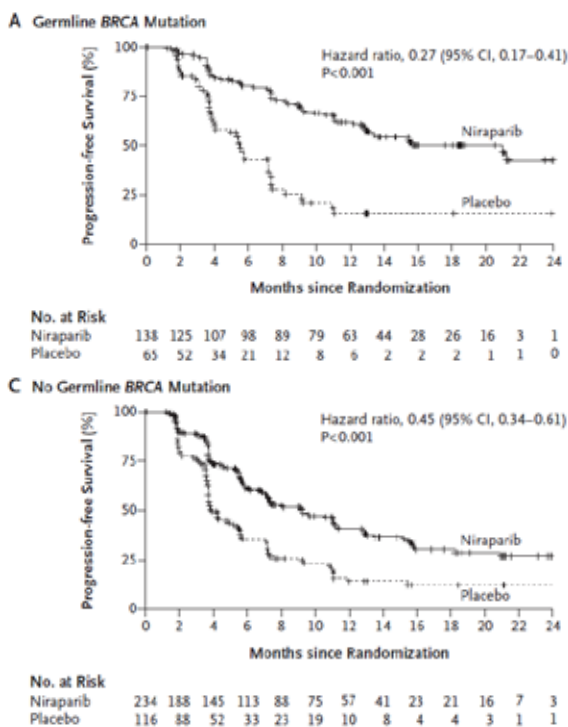


Fig.2: Key efficacy results from the NOVA phase III trial



Source: NEJM

### Highlights from day 2

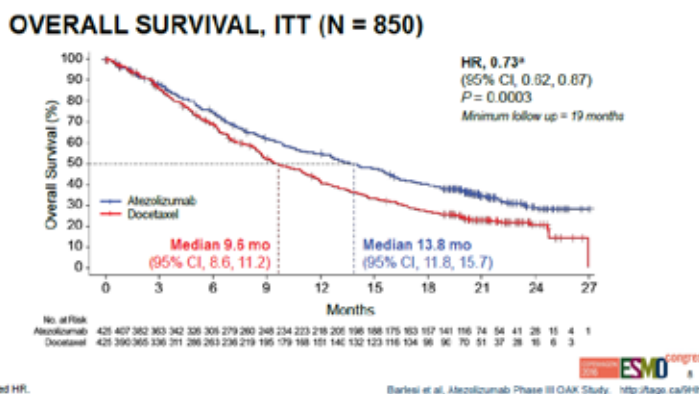
Sunday clearly put immuno-oncology drugs on the forefront and a full presidential symposium was dedicated to the key publications in this category.

Anecdotally, the *Daily Reporter* which is the internal newspaper of the ESMO congress released every day put on its front page today i.e. took as the key message from yesterday's presentations the results with ipilimumab in adjuvant melanoma. This is illustrative of the central position already occupied by I.O. at ESMO while we are still at the beginning of their journey. It is also objective to say that toxicity (15 out of 18 patients stopped treatment before the end of the study in OpACIN for instance) does not look like an issue. However, in less prestigious satellites, the question of cost was raised and already today is creating big inequities across regions and countries: "high cost is a barrier" clearly stated an Italian oncologist that was talking about I.O/I.O combinations in lung cancer. One key question remains: who should I give each drug to, how and how long? Some speakers suggested that in real life, they might decide to give some I.O drugs less long than showed in clinical trials because they act as gate-openers and their effect usually goes beyond treatment interruption.

So, that said, there were several interesting presentations that overall suggested the marked influence of PD-1 and PD-L1 agents in many solid tumor types. It is worth saying that nivolumab and pembrolizumab were the more popular drugs discussed, reflecting their advance in several settings. However, it is fair to say that at least at the time of the conclusion of many discussions hopes about

combinations to reach an even greater level of response and efficacy were often formulated, for instance in TNBC or in kidney cancer but also by discussants in the Presidential Symposium. So let's say a few words about each of the three key presentations with the angle of learning for the European players of our coverage. From that perspective, of course, OAK first phase III data were the most significant and we would say also the less debated results (based on overall survival) as atezolizumab clearly showed superiority over Taxotere across the board i.e. irrespectively of patient characteristics and subgroup analysis and notably between squamous and non-squamous NSCLC and between PD-L1 positive and negative (although very expressers benefited even more than others). Curves separated early and in the end atezolizumab demonstrated median OS of 13.8 months vs 9.6 months for docetaxel (HR=0.73, p=0.0003) and this came with overall good safety profile with 15% grade 3-4 adverse events related to the treatment vs 43% for the taxane. We would note that like other PD-1 drugs previously, PFS did not show statistical difference between arms.

**Fig.3: OS results from first OAK phase III data analysis**



Source: Roche, ESMO 2016

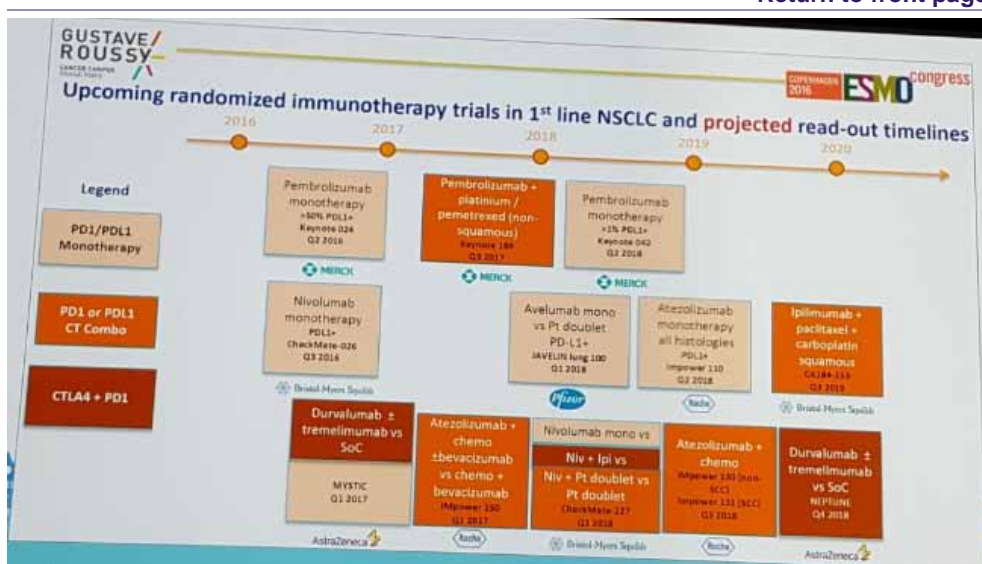
In conclusion, we would say that atezolizumab appears as effective as PD-1 drugs already approved in the same setting of 2L/3L NSCLC with maybe a clearer advantage in terms of persistence of efficacy across various populations obtained from one single trial with 1,225 patients and with a Q3w treatment interval (vs Q2W for nivolumab). As a reminder, Roche is expecting the FDA to act on Tecentriq's first BLA in advanced PD-L1 positive NSCLC by the end of next week and with pembrolizumab's success in 1L, is expecting to get a significant share of the 2L/3L setting with atezolizumab monotherapy while continuing to explore combinations to compete in 1L.

So, precisely, now moving to KEYNOTE-024 which is the study that investigated pembrolizumab against platinum-based therapies in 1L NSCLC with PD-L1 expression of 50% or more, needless to say that the results are outstanding with HR of 0.50 for median PFS and 0.60 for median OS. Overall response rate also clearly favoured pembrolizumab (45% vs 28%) with 6 complete responders and with the exception of people that never smoke (with no difference), all subgroups benefited from pembrolizumab. As with atezolizumab, safety was also in favour of the PD-1, notably grade 3-4 adverse events with an incidence of 26% (vs 51%).

However, what was very interestingly raised by discussant Jean-Charles Soria from IGR, who noted the unprecedented ORR of 45% for a PD-1 in monotherapy and the outstanding results in squamous cell lines (HR=0.35), is the limited population addressed by the study. Not only PD-L1 high expressers do represent only a quarter to a third of NSCLC patients but once the exclusion criteria are considered (no ALK or EGFR mutation, no brain metastasis, etc...), it is only 10-15%. This is how Merck came from 1,934 patients screened down to 305 randomized patients.

So, on one hand, the results are clearly suggestive of a benefit of using I.O. in 1L NSCLC maybe even vs 2L/3L but so far the evidence is data-based in only a small subset of the total population. This leaves room for new agents and combinations to take a greater part of the 1L NSCLC pie. CHECKMATE-227 and MYSTIC have been mentioned more particularly but the list is fairly long (see Fig.4).

**Fig.4: Upcoming data with IO drugs in NSCLC**



Source: ESMO 2016, JC Soria

Lastly, we conclude with the CHECKMATE-026 trial which was a failure for BMS in demonstrating benefit for nivolumab in 1L PD-L1 positive NSCLC vs chemotherapy. It was a complete failure as all parameters favoured the CT arm which includes median PFS (HR=1.15), median OS (HR=1.02) and ORR (26.1% vs 33.5%). Some imbalances between groups (more female and more PD-L1 high expressers in the CT arm) may have participated to the failure but the magnitude of the failure suggests further investigation although. When put together with KEYNOTE-024 however, the results are suggestive of a meaningful effect of a PD-1 targeting agent only in high PD-L1 expressers and highly selected populations (like Merck did but much less so BMS). Good thing is that it leaves a very significant part of the NSCLC market still open in 1L to new options. As illustrated above, several combinations are currently being tested that will start reporting results in 2017 or in 2018 if PFS proves insufficient.

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## Healthcare

**Genmab**

Price DKK1,136

**Priority review obtained... Now expecting a label expansion in Q1 2017****Fair Value DKK1600 (+41%)****BUY**

Bloomberg	GEN DC
Reuters	GEN.CO
12-month High / Low (DKK)	1,266 / 593.5
Market Cap (DKKm)	68,443
Avg. 6m daily volume (000)	385.6

	1 M	3 M	6 M	31/12/15
Absolute perf.	8.7%	-4.6%	23.1%	23.8%
Healthcare	-2.8%	-5.0%	0.1%	-10.0%
DJ Stoxx 600	-3.1%	5.4%	3.5%	-7.2%

	2015	2016e	2017e	2018e
P/E	NS	NS	NS	55.0x
Div yield (%)	NM	NM	NM	NM

**ANALYSIS**

- GEN and JNJ have announced that the FDA has granted a priority review to the supplemental BLA involving the use of daratumumab 1/ in combination with CELG's Revlimid (lenalidomide) plus dexamethasone, and 2/ for the treatment of patients with myeloma who received at least one prior therapy. As such, **a decision is expected no later than 17th February 2017.**
- **We believe the label expansion could be granted slightly before this date** in light of the quality of the clinical package (see our recent research report for further details), as well as the recent granting of a Breakthrough Therapy Designation (BTD). Especially since early decisions have become more and more frequent in oncology: Blincyto, Keytruda, Opdivo, and even "dara" back in November 2015.
- But great news never comes alone, as the US regulator also granted a standard review period for the use of "dara" as part of another combination regimen (pomalidomide with dexamethasone) in more advanced lines of treatment (3L and above). While there is no priority review here, we consider this very positive, obviously since it was not widely expected, but also because it would further expand the potential window of possibilities.

**VALUATION**

- BUY reiterated with a FV of DKK1,600.

**NEXT CATALYSTS**

- 10th November 2016: Capital Market Day.
- 9th December 2016: R&D/ASH Day

[Click here to download](#)Mickael Chane Du, [mchanedu@bryangarnier.com](mailto:mchanedu@bryangarnier.com)



Healthcare

**Innate Pharma**

Price EUR11.01

Let's wait for the SITC to get a view of the efficacy profile of liri/nivo

Fair Value EUR18 (+63%)

BUY

Bloomberg	IPH.FP
Reuters	IPH.PA
12-month High / Low (EUR)	14.5 / 9.5
Market Cap (EURm)	594
Avg. 6m daily volume (000)	262.7

**ANALYSIS**

- BMS presented the detailed safety data from its Phase I evaluating lirilumab in combination with nivolumab in a range of different solid tumours. Unsurprisingly, the dataset confirmed our (positive view) on this aspect of the combination.

**Table 3. All TRAEs and TRAEs Reported in ≥ 5% of All Patients in CA223-001**

Patients With ≥ TRAE, n (%)	Lirilumab 0.1 mg/kg + Nivolumab 3.0 mg/kg n = 4		Lirilumab 0.3 mg/kg + Nivolumab 3.0 mg/kg n = 16		Lirilumab 1.0 mg/kg + Nivolumab 3.0 mg/kg n = 15		Lirilumab 3.0 mg/kg + Nivolumab 3.0 mg/kg n = 124		All Patients N = 159	
	Any Grade	Grade 3/4 <sup>a</sup>	Any Grade	Grade 3/4 <sup>a</sup>	Any Grade	Grade 3/4 <sup>a</sup>	Any Grade	Grade 3/4 <sup>a</sup>	Any Grade	Grade 3/4 <sup>a</sup>
Any TRAE	4 (100)	2 (50.0)	15 (93.8)	2 (12.5)	14 (93.3)	3 (20.0)	81 (65.3)	17 (13.7)	114 (71.7)	24 (15.1)
TRAEs in ≥ 5% of all patients										
Fatigue	2 (50.0)	0	5 (31.3)	0	4 (26.7)	0	22 (17.7)	0	33 (20.8)	0
Pruritus	2 (50.0)	0	3 (18.8)	0	6 (40.0)	0	19 (15.3)	0	30 (18.9)	0
Infusion-related reaction	1 (25.0)	0	1 (6.3)	0	7 (46.7)	0	19 (15.3)	0	28 (17.6)	0
Rash	1 (25.0)	0	5 (31.3)	0	4 (26.7)	0	16 (12.9)	0	26 (16.4)	0
Diarrhea	0	0	0	0	3 (20.0)	1 (6.7)	10 (8.1)	0	13 (8.2)	1 (0.6)
Arthralgia	0	0	3 (18.8)	0	4 (26.7)	0	6 (4.8)	0	13 (8.2)	0
Amylase increased	0	0	2 (12.5)	0	1 (6.7)	0	9 (7.3)	4 (3.2)	12 (7.5)	4 (2.5)
Maculopapular rash	0	0	2 (12.5)	0	1 (6.7)	1 (6.7)	9 (7.3)	1 (0.8)	12 (7.5)	2 (1.3)
Nausea	1 (25.0)	0	2 (12.5)	0	2 (13.3)	0	7 (5.6)	0	12 (7.5)	0
Appetite decreased	2 (50.0)	0	0	0	1 (6.7)	0	6 (4.8)	0	9 (5.7)	0
Pyrexia	0	0	0	0	0	0	8 (6.5)	0	8 (5.0)	0

- But again, efficacy is of essence. As such, we'll have to wait for the SITC congress to get some colour on the efficacy profile of liri/nivo in solid tumours. And given the design of the trial, we believe some overall survival (OS) data could be presented.
- Note that 27% of the patient population was continuing the treatment at the end of August 2016 and the median duration was 14-58 weeks. However, we find it hard to extrapolate any potential efficacy analysis given the lack of details (median number of prior therapies (3?), which dose caused the most disease progression? which cancer was the most represented? etc.).

**VALUATION**

- BUY reiterated with a FV of EUR18.

**NEXT CATALYSTS**

- 9-13th November 2016: Presentation of liri/nivo's efficacy data in different solid tumours.

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Healthcare

**Nicox**

Price EUR8.33

**AC-170 got a CRL... We see the glass as half full**

Fair Value EUR14 (+68%)

CORPORATE

Bloomberg	COX FP
Reuters	NCOX.LN
12-month High / Low (EUR)	13.4 / 6.0
Market Cap (EURm)	208
Avg. 6m daily volume (000)	281.3

	1 M	3 M	6 M	31/12/15
Absolute perf.	-17.8%	-34.2%	16.7%	-8.7%
Healthcare	-2.8%	-5.0%	0.1%	-10.0%
DJ Stoxx 600	-3.1%	5.4%	3.5%	-7.2%

	2015	2016e	2017e	2018e
P/E	NS	NS	NS	NS
Div yield (%)	NM	NM	NM	NM

**ANALYSIS**

- Nicox announces this morning that it has received a Complete Response Letter (CRL) from the FDA regarding the potential approval of AC-170 (eye drop formulation of cetirizine developed for the treatment of ocular itching associated with allergic conjunctivitis). Importantly, the regulator stated reason for the CRL pertains solely to a Good Manufacturing Practice (GMP) inspection at a third party facility producing the active pharmaceutical ingredient and supplying it to the manufacturer of the finished product.
- This is obviously unfortunate, but we see two good news behind this decision: 1/ the letter just mentioned manufacturing issues and the regulator did not request any additional clinical or non-clinical data to strengthen the NDA; 2/ because of this delay in the approval, the potential related milestone payment to Acix shareholders is more likely to be USD10m (vs USD35m should a green light be granted before December 1<sup>st</sup> 2016)... Thus reducing the associated dilution to 5% rather than 17% on the basis of the current share price.

**VALUATION**

- We stick to our FV of EUR14 knowing that AC-170 stands for roughly EUR2.5 per share.

**NEXT CATALYSTS**

- Q4 16/Q1 16: Potential update on latanoprostene bunod's CRL.

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Healthcare

**Novo Nordisk**

Price DKK270.30

**Unexpected delay for ultra-fast acting insulin in the US**

Fair Value DKK355 vs. DKK360 (+31%)

**NEUTRAL**

Bloomberg	NOVOB DC
Reuters	NOVOB.CO
12-month High / Low (DKK)	404.2 / 270.3
Market Cap (DKK)	543,996
Avg. 6m daily volume (000)	2,990

	1 M	3 M	6 M	31/12/15
Absolute perf.	-11.0%	-26.1%	-26.9%	-32.4%
Healthcare	-2.8%	-5.0%	0.1%	-10.0%
DJ Stoxx 600	-3.1%	5.4%	3.5%	-7.2%

	2015	2016e	2017e	2018e
P/E	19.9x	17.4x	16.4x	15.7x
Div yield (%)	2.4%	2.6%	2.7%	2.9%

**ANALYSIS**

- Very unexpectedly, Novo-Nordisk announced on Friday after market close that it had received a complete response letter (CRL) from the FDA for its BLA for the ultra-fast acting insulin known as Fiasp. The group mentions that the FDA is asking for more information about the assay for immunogenicity and clinical pharmacology data used in the trials before completing the review. It looks like it might require some new work, if not new trials.
- This was not at all anticipated and is likely to come as an unwelcome surprise for the market at a time when there were already a lot of questions about other parts of the portfolio, including basal insulins and basal/GLP1 combination after recent payer decisions and regulatory delays in the US respectively.
- Fiasp was leading the pack in the field of ultra-fast acting insulins by about two years when compared to Lilly's BC lispro (due to enter phase III in early 2017). Obviously, this is good news for Lilly (and its partner Adocia), which – if everything has been carried out seriously – might close the gap with Novo-Nordisk by several months.

**VALUATION**

- We had expected Fiasp to come to market by the end of 2016 and this is going to be significantly delayed at least in the US (but which is the main market). That said, we cautiously took a 70% PoS and only USD80m for 2017 so the adjusted sequence of sales has a limited impact on our FV.
- Beyond numbers, sentiment is worsening about Novo-Nordisk that proves difficult to translate still very good science in growing numbers as it was used to doing in the past. We maintain our Neutral recommendation.

**NEXT CATALYSTS**

- 28th October 2016: Third-quarter results

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TMT

**Worldline**

Price EUR26.47

We consider the current share price as a good entry point

Fair Value EUR31 (+17%)

**BUY**

Bloomberg	WLN.FP
Reuters	WLN.PA
12-month High / Low (EUR)	29.1 / 19.0
Market Cap (EUR)	3,498
Ev (BG Estimates) (EUR)	3,039
Avg. 6m daily volume (000)	72.10
3y EPS CAGR	11.2%

After losing 9% since its peak on 2nd September, we believe the current price is attractive enough to play positive momentum and more visibility in a couple of days. This should begin with the Q3 release on 19th October (the group should give FY guidance including the Equens/Paysquare and KB deals, in order for the consensus to officially integrate them into its model), and Atos' capital market day on 8th November). At 9.7x EV/EBITDA over 12 rolling months, we advise investors to target 12x. Then, in the coming months, the group has the means to sign a new acquisition to give even more upside to this multiple. We maintain our Buy recommendation and FV of EUR31.

	1 M	3 M	6 M	31/12/15
Absolute perf.	-6.5%	5.3%	15.3%	10.9%
Softw. & Comp.	-1.1%	16.9%	12.8%	6.6%
DJ Stoxx 600	-3.1%	5.4%	3.5%	-7.2%

**ANALYSIS**

Given the underperformance of the Worldline share in recent weeks (-9% since its highest level on 2nd September), we see the current price as very attractive (upside of 17%).

**2016e: 1) Q1:** 9.5% underlying revenue growth and -3% from the VOSA contract = +6.5% lfl; **2) Q2:** 8.6% underlying revenue growth and -3% from the VOSA contract = +5.6% lfl (comparison basis effect). This means +6% lfl over H1 2016; **3) Q3:** 7-8% underlying revenue growth, -3% from the VOSA contract and -5% from the radar contract = -1-0% lfl; **4) Q4:** 8% in underlying revenue growth and -5% from the radar contract = +3% lfl. This means 8% in underlying revenue growth over FY 2016 = +3.5% lfl over FY 2016. **So, Worldline is able to generate 7-8% underlying revenue growth. We do not expect any disappointment on margins** (as for Atos, management has an excellent track record on the operating level, and is good at cutting costs).

**2017e: 1) H1:** 7% underlying revenue growth, -5% from the radar contract = +2% lfl. **2) H2:** 7% underlying revenue growth - 0% (end of contract losses) = +7% lfl. **This points to 7% underlying revenue growth over the full year 2016, i.e. +4.5% lfl over FY 2017. As this is a fixed cost business, there will be an operating leverage (margin improvement).**

**We strongly believe that WLN will give FY guidance including the Equens/Paysquare and KB deals during the next set of figures, namely Q3 revenue 2016 on 19th October. 1) Q3 revenue** will be the lowest growth of the year because of the first radar contract loss impact (BG estimate: EUR293.4m, -0.9% Y/Y lfl in Q3), however we expect Q4 to resume growth with +3% lfl; **2) the consensus will at last integrate this into their models and this should drive EPS upwards and of course target prices** (our FV of EUR31 already integrates these two deals).

**Atos will hold an investor day on 8th November** to give mid-term guidance (2019 or 2020 in our view), which should include a part dedicated to Worldline. It should show organic revenue growth of 5-7% and a strong margin improvement (strong synergies from the Equens deal as of 2018).

**What is not integrated into the current share price ? 1) the next M&A deal** (probably a platform from a bank subsidiary in Central Europe or Eastern Europe); **2) the strong margin improvement we expect in 2018 and 2019 linked to the synergies from Equens.**

**Simulation: Worldline with consolidation of Equens and KB and the end of the French radar contract**

EURm	2016e	2017e	2018e	2019e
Revenue	1,311.9	1,607.7	1,685.6	1,767.2
Lfl growth	3.5%	4.5%	4.8%	4.8%
EBITDA	261.8	320.6	348.0	374.0
Margin	20.0%	19.9%	20.6%	21.2%
Synergies	4.0	20.0	40.0	45.0
EBITDA after synergies	265.8	340.6	388.0	419.0
Margin	20.3%	21.2%	23.0%	23.7%
Current EBIT	201.0	251.7	295.1	335.6
Margin	15.3%	15.7%	17.5%	19.0%
EBIT	165.7	235.8	281.3	327.7
Margin	12.6%	14.7%	16.7%	18.5%
Restated attrib. net income	134.5	163.7	188.1	211.4

Source: Bryan, Garnier & Co ests.



## Worldline's multiples based on our simulation

x	2016e	2017e	2018e
EV/Sales	2.4	1.8	1.8
EV/EBITDA	12.0	9.0	9.0
EV/current EBIT	15.9	12.1	12.1
P/E	26.6	21.8	21.8

Source: Bryan, Garnier & Co ests.

## VALUATION

- Our FV of EUR31 integrates the Equens/Paysquare and KB deals (upside of 17%) but the consensus has yet to do this.
- Over 2016 the share is fully valued at 12x EBITDA (i.e. consistent with its positioning as a physical PSP), however on 12 rolling months it is at only 9.7x (we see upside up to 12x). And, of course, it is even more attractive in 2017 at 9.0x.
- We believe Worldline could step up M&A activity again. This could offer even higher leverage to EV/Ebitda (to target 12x).

## NEXT CATALYSTS

- Q3 revenue: 19th October (after trading).
- Atos' Capital Market Day: 8th November.

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## Construction &amp; Building Materials

**LafargeHolcim**

Price CHF51.90

**Another step in the divestment process**

Fair Value CHF60 (+16%)

BUY-Top Picks

Bloomberg	LHN.VX
Reuters	LHN.VX
12-month High / Low (CHF)	57.7 / 34.1
Market Cap (CHFm)	31,499
Avg. 6m daily volume (000)	1,730

	1 M	3 M	6 M	31/12/15
Absolute perf.	-1.9%	31.2%	14.5%	3.2%
Cons & Mat	-2.9%	12.8%	8.0%	3.9%
DJ Stoxx 600	-3.1%	5.4%	3.5%	-7.2%

	2015	2016e	2017e	2018e
P/E	39.9x	22.3x	15.7x	11.4x
Div yield (%)	2.9%	3.2%	3.5%	3.8%

**ANALYSIS**

- LafargeHolcim has signed an agreement with a company from the Hurtado Vicuna Group, for the divestment of its 54.3% stake in the Chilean company Cementos Polpaico (2.3 mt of cement capacity) for a EV of -CHF120m. This is equivalent to CHF220m for 100%, i.e. -100 USD per ton
- The deal is structured through a public tender offer to all shareholders of Cemento Polpaico. We understand the operation is likely to be completed in 2017. Once the deal is completed, LafargeHolcim will not be exposed to Chili anymore.
- The size of the deal is modest for a group like LafargeHolcim. It is nevertheless another step in the right direction. The group has already exceeded its CHF3.5bn disposal target for 2016 and has extended it to CHF5bn by the end of next year.
- Besides, exiting Chile is unlikely to be perceived as negative. Indeed, Chili is not especially a dynamic country currently. According to the International Cement Review, the top three players have reported a 3.7% y/y increase in Sales in H1 2016, the lowest growth rate in three years.

**VALUATION**

- CHF60 FV derived from the application of historical multiples to of 2018 estimates, discounted back

**NEXT CATALYSTS**

- Q3 results on 4 November 2016. Capital Market Day on 18 November 2016

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## BG's Wake Up Call

# Bryan Garnier stock rating system

For the purposes of this Report, the Bryan Garnier stock rating system is defined as follows:

### Stock rating

BUY	Positive opinion for a stock where we expect a favourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential upside based on valuation), but also takes into account a number of elements that could include a SWOT analysis, momentum, technical aspects or the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.
NEUTRAL	Opinion recommending not to trade in a stock short-term, neither as a BUYER or a SELLER, due to a specific set of factors. This view is intended to be temporary. It may reflect different situations, but in particular those where a fair value shows no significant potential or where an upcoming binary event constitutes a high-risk that is difficult to quantify. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.
SELL	Negative opinion for a stock where we expect an unfavourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential downside based on valuation), but also takes into account a number of elements that could include a SWOT analysis, momentum, technical aspects or the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

### Distribution of stock ratings

BUY ratings 56.5%

NEUTRAL ratings 31.8%

SELL ratings 11.7%

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