4th November 2016

Sector View

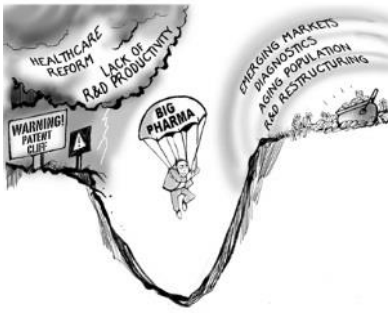
Pharmaceuticals

Safety issues arise from ACE910's trial… Do not rush to make a judgement

	1 M	3 M	6 M	31/12/15
Healthcare	-7.9%	-12.6%	-5.9%	-16.3%
DJ Stoxx 600	-3.4%	-1.2%	-1.2%	-9.4%

*Stoxx Sector Indices

Companies covered				
ACTELION		**NEUTRAL**		**CHF180**
Last Price	CHF137,1	*Market Cap.*	CHF14,774m	
ASTRAZENECA		**BUY**		**5220p**
Last Price	4434,5p	*Market Cap.*	*GBP56,098m*	
BAYER		**NEUTRAL**		**EUR98**
Last Price	EUR88,75	*Market Cap.*	*EUR73,392m*	
GLAXOSMITHKLINE		**BUY**		**1930p**
Last Price	1554p	*Market Cap.*	*GBP75,775m*	
GRIFOLS		**NEUTRAL**		**EUR20**
Last Price	EUR17,655	*Market Cap.*	*EUR10,974m*	
IPSEN		**BUY**		**EUR72**
Last Price	EUR61,32	*Market Cap.*	*EUR5,113m*	
NOVARTIS		**NEUTRAL**		**CHF81**
Last Price	CHF68,95	*Market Cap.*	*CHF181,140m*	
NOVO NORDISK		**NEUTRAL**		**DKK270**
Last Price	DKK236,8	*Market Cap.*	*DKK476,575m*	
ROCHE HOLDING		**BUY**		**CHF285**
Last Price	CHF222,7	*Market Cap.*	*CHF156,461m*	
SANOFI		**NEUTRAL**		**EUR84**
Last Price	EUR72,29	*Market Cap.*	*EUR93,191m*	
SHIRE PLC		**BUY**		**6800p**
Last Price	4539p	*Market Cap.*	*GBP41,010m*	
SOBI		**SELL**		**SEK90**
Last Price	EUR98,2	*Market Cap.*	*EUR26,552m*	
UCB		**NEUTRAL**		**EUR80**
Last Price	EUR59,78	*Market Cap.*	*EUR11,628m*	



Some patients in ROG's trial evaluating ACE910 have experienced severe thrombotic events. Given yesterday's share price reactions, the Street seems to have taken for granted that such side effects could be associated to the compound. However, it is worth mentioning that these patients were previously treated with bypassing therapies that are known to increase thrombotic risks. We believe the phase III results expected by year-end are likely to bring some answers and as a consequence we reiterate our hierarchy for the haemophilia field.

ANALYSIS

- **Severe thrombotic AE seen in ACE910's trial**. Roche revealed that four patients from one of its trial evaluating ACE910 experienced severe thrombotic adverse events (two thromboembolic events and two cases of thrombotic microangiopathy). As a result, the company has issued dear investigator letters (DILs) 1/ to better monitor thrombotic markers, and 2/ to implement further safety measures. As the patients included were said to be previously treated with bypassing therapies (Feiba, NovoSeven), we understand that the trial is the one involving patients who developed inhibitors.
- **Do not rush to make judgement.** Given yesterday's share price reactions, the Street seems to have taken for granted that these side effects are ACE910-related, and especially since the trial involves four active arms testing different doses of this drug without comparative arm. But there is no certainty here in our view as the patients used to be treated with either SHP's Feiba or Novo's NovoSeven, and both of them are known to increase thrombotic risks (Diringer et al, 2008; Aledort et al, 2004).
- **But we still believe ACE910 is unlikely to fully address the whole Haemophilia A market.** Although we would not suddenly bark with the hounds and suggest that ACE910 carries high risk of failure, we remain cautious about the overall safety profile of the drug (severe AEs like appendicitis and mesenteric hematoma being observed in a small phase I; and although they apparently non-neutralizing ones, some patients developed antibodies against the molecule). No more, no less than we were before and as described in our recent report about Haemophilia. So far, we can just reiterate our belief that FVIII will remain the SOC despite ACE910's competition and thus will remain the standard of care for patients with no inhibitors.
- **First phase III results with ACE910 in patients with inhibitors are expected by year end and are likely to give some answers… As a consequence, we stick to our hierarchy in the haemophilia field**. As a reminder, we foresee peak sales of USD2.0bn for ACE910 (of which USD1.5Bn should stem from patients with inhibitors) although we have so far applied a 40% probability of success, which is severe for a drug in phase III but reflects the risk associated with a mechanism of action. As soon as the first results are out and we will balance PoS and PS accordingly. Compared to our recent report and following disappointing third-quarter figures, note that we have adjusted downwards our numbers on Novo's Haemophilia franchise (DKK2,285m in Q3 vs DKK2,530m in Q2 and DKK2,836m in Q1). We remain more pessimistic than CS about NovoSeven that we see sales halved between 2015 and 2020.

NEXT CATALYSTS

- Q4 16: phase III results of ROG's ACE910 for the treatment of haemophilia A patients with inhibitors.

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Analyst :
Mickael Chane Du
33(0) 1 70 36 57 45
mchanedu@bryangarnier.com

Sector Team :
Eric Le Berrigaud
Hugo Solvet
Marion Levi

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London
Beaufort House
15 St. Botolph Street
London EC3A 7BB
Tel: +44 (0) 207 332 2500
Fax: +44 (0) 207 332 2559
Authorised and regulated by the Financial Conduct Authority (FCA)

Paris
26 Avenue des Champs Elysées
75008 Paris
Tel: +33 (0) 1 56 68 75 00
Fax: +33 (0) 1 56 68 75 01
Regulated by the Financial Conduct Authority (FCA) and the Autorité de Contrôle prudential et de resolution (ACPR)

New York
750 Lexington Avenue
New York, NY 10022
Tel: +1 (0) 212 337 7000
Fax: +1 (0) 212 337 7002
FINRA and SIPC member

Munich
Widenmayerstrasse 29
80538 Munich
Germany
+49 89 2422 62 11

New Delhi
The Imperial Hotel Janpath
New Delhi 110 001
Tel +91 11 4132 6062
+91 98 1111 5119
Fax +91 11 2621 9062

Geneva
rue de Grenus 7
CP 2113
Genève 1, CH 1211
Tel +4122 731 3263
Fax+4122731 3243
Regulated by the FINMA