White Paper – Productive Innovation Index – 2014

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"We are what we repeatedly do. Excellence, then, is not an act, but a habit." **Aristotle**

A casual observer might have noted that only 27 NMEs/BLAs were granted by the FDA last year, a significant fall from the 16-year high of 39 approved the year before. One might question whether R&D productivity is faltering again and declining towards the low levels seen between 2000 and 2005. Upon closer inspection, however, the trend in drug productivity over the last five years is still greater than at any time since the 1990s.

Another facet to be cautiously optimistic about is the industry's productive innovation. It is improving significantly. Companies are aware now more than ever that launchability is only a surrogate endpoint and not an end in itself. Delivering value to the market is…

The Productive Innovation Index (PII) measures how well a company performs in bringing a medicine to market successfully. The ranking is in its fourth year of publication, and expands on previous years by including assessments for the top 30 drug companies. Some achieve a consistently high rank, year-on-year, while others have surged up the rankings.

2014	Company	Change	2013
1	Johnson & Johnson	-	1
2	Novartis	+5	7
3	Roche	-	3
4	Bristol-Myers Squibb	+5	9
5	GlaxoSmithKline	+3	8
6	Merck & Co	-2	4
7	Bayer	+10	17
8	Sanofi	-3	5
9	Abbott Laboratories/AbbVie	+1	10
10	Boehringer Ingelheim	+10	20
11	Novo Nordisk	New	
12	Pfizer	-1	11
13	Biogen Idec	+6	19
14	Amgen	-12	2
15	AstraZeneca	-	15
16	Celgene	New	
17	Lilly	-11	6
18	Gilead Sciences	-2	16
19	Otsuka Holdings	New	
20	Baxter International	New	
21	Takeda	-9	12
22	Shire	-4	18
23	Astellas	-9	14
24	Merck KGaA	-3	21
25	Eisai	New	
26	Actelion	-2	24
27	Lundbeck	-14	13
28	UCB	-6	22
29	Regeneron Pharmaceuticals	New	
30	Teva	-7	23

This white paper provides some 'behind the scenes' illumination – why these companies are great at launching great drugs, and thereafter gaining good penetration and market share. The top 10 performers of the 2014 Productive Innovation Index are covered in some detail below.

1. J&J retains first place due to significant successes in CNS, oncology, immunology and metabolism. Most notable in 2013 was the launch of Imbruvica (ibrutinib), which achieved breakthrough designation (BTD) for mantle cell lymphoma. It also launched the first in class Invokana (canaglifozin) for type 2 diabetes. Both have already registered strong sales. Also helping J&J stay at the top are higher than average investment in R&D, six NME/BLA approvals in the last three years, a significant amount of revenue growth from recent launches and that its strong pipeline also contains one other drug granted a BTD. There were no significant negatives other than a negative opinion from the FDA regarding Xarelto in ACS.
2. Novartis, now second, has recovered from sub-par performances in the cardiovascular and metabolism area and done much to offset Diovan patent expiry, with some strong launches in critical care and oncology. Its sales growth comes from a range of young products and its focus on rapid first-to market strategies seems to be working. It has one of the largest industry pipelines that include three drugs with BTD status, including serelaxin, although at the time of writing, Novartis had received a negative opinion by the CHMP for this in heart failure.
3. Roche has cemented its position in the top three with groundbreaking launches in 2013 with Kadcyla and Gazyva, the first therapy with breakthrough designation to be approved by the FDA. Roche is one of the biggest investors in R&D and subsequently has a burgeoning pipeline. Alectinib, for non-small cell lung cancer (NSCLC), was also granted BTD status last year. The one major negative for Roche was the discontinuation of aleglitazar from phase III, the latest in a string of late-stage failures in the cardiovascular and metabolism area.
4. Bristol-Myers Squibb has climbed several places to position number four thanks to launches in immunology and oncology and the hybridisation of both areas to form one of the leading immuno-oncology franchises in the industry. Although BMS did not have any NME/BLA approvals last year, it has seen very significant growth from new products Sprycel, Yervoy and Nulojix to offset loss of patent protection for key products in the cardiovascular franchise. Its challenges in that area continue due to limited traction with its new blood thinner, Eliquis, which was launched in 2012.
5. GlaxoSmithKline could be much higher in the rankings were it not for a large proportion of sales coming from mature products in one disease area and the discontinuation of darapladib in phase III. Yet, it has the largest number of NME/BLA approvals of anyone in the rankings over the last three years and is fast becoming a leader in oncology with three recent launches, and GSK is attempting to consolidate its lead in respiratory disease through the launches of Breo Ellipta and Anoro Ellipta. GSK also has a diverse and large pipeline that contains no less than three drugs with a BTD.
6. Merck and Co had a year of transition to land in sixth. On the upside, it has strong immunology and infectious disease franchises with Remicade and Gardasil contributing double-digit growth. Merck also has two drugs with BTD status and a healthy pipeline. Its partnership deals in diabetes with Pfizer and Abide will also help to build on Merck's Januvia franchise. On the downside, Merck finds itself without many new products with strong growth to offset a string of recent patent expiries. Tredaptive (for dyslipidaemia) being pulled from the market due to safety concerns and a late stage failure for preladenant in Parkinson's disease have not helped either, but a number of filings for new products look set to allow Merck to enter a new growth phase.
7. Bayer jumped up 10 places to seventh, and is a company much transformed compared to a decade ago when the Baycol withdrawal was still relatively recent history. Since then, it has gone through a big transition and focussed exclusively on oncology, CVM, haematology and gynaecology and had a hugely successful partnership with Onyx. Bayer has had six NME/BLA approvals over the last three years. Sales of Eylea, Stivarga, Xarelto, Xofigo have all contributed to very strong growth and this has allowed Bayer to invest a significant portion of revenue back into R&D. Adempas was also approved last year and is a first in class agent for the treatment of PAH.
8. Sanofi drops a couple of places to eighth. Like Merck, Sanofi is going through a period of turbulence. Sanofi has had five consecutive quarters of sales erosion to Plavix, Avapro and Eloxatin. 2013 also saw lower than expected financial results which were partly influenced by the pulled filing of Lyxumia in the US and dropping cancer drugs iniparib and fedratinib, and the anticoagulant otamixaban from development after negative phase III trials. A silver lining has been the high-performing Genzyme division, which includes Aubagio for MS, which has provided significant growth. Sanofi has three approvals over the last three years and a full late-stage pipeline for pharmaceuticals and vaccines.
9. After the spin-off from Abbott Laboratories, AbbVie in ninth place, has relied heavily on Humira sales, a $10billion drug launched over a decade ago, to provide the revenue it needs for transforming into an immunology, CNS, oncology and infectious disease R&D powerhouse. While there have been no new NMEs/BLAs in the last three years, it has built a balanced development pipeline numbering over 20 drugs and containing a combination drug for HCV with BTD.
10. Squeezing into the last spot of the top 10, Boehringer Ingelheim has had a number of successful launches in recent years with both Pradaxa and Trajenta contributing strong sales and both Gilotrif and Striverdi approved in 2013. BI has built a strong business around COPD, cardiovascular disease, infectious disease and oncology, and thanks to above average investment in R&D, has an extensive late-stage pipeline. The pipeline also contains volasertib, which was granted BTD status. It wasn't all positive news though with the parting of ways with Lilly over a diabetes programme.

Beyond the top 10, there are also a number of companies that, while they didn't break into the upper echelons, do provide noteworthy examples of productive innovation.

Gilead's success in viral disease:
Once again Gilead has demonstrated its mastery in developing combination pills containing multiple anti-viral therapies – it already had significant success in HIV and HBV with this approach and this has translated most recently to BTD status for Solvadi, a new hepatitis C drug that some analysts say could become a blockbuster and a new standard of care.

Novo Nordisk's domination in diabetes:
Novo Nordisk continues to dominate diabetes by covering every patient segment with products ranked 1 or 2 in oral therapy or insulins. For a company to show such depth and breadth in one therapy area demonstrates an intelligent approach towards innovation, enabling it to commandeer and capitalise on this ever-growing disease, seeing it making its debut on the PII.

Celgene's success with once unloved drugs that work in oncology:
Celgene has shown exceptional dumpster diving ability by taking thalidomide and redeveloping it into a set of new drugs for oncology – Revlimid and Pomalyst, both effective treatments in multiple myeloma. Also the company has shown an instinctive foresight by taking on Abraxane, originally passed over by AZ. It recognised Abraxane's latent potential by securing first-line approvals in pancreatic cancer (a very difficult to treat tumour) last year, after a prior approval for first-line NSCLC in 2012, thereby securing 90 per cent sales growth over 12 months.

Biogen's continued success in multiple sclerosis:
Biogen Idec have gone from strength to strength in multiple sclerosis despite the presence of increasing and continuously evolving competition. Its leadership has been maintained over almost two decades with the initial launch of Avonex back in 1996, then Tysabri in 2005, and most recently, Tecfidera launching last year and already well on the way to achieving blockbuster status.

What these companies all have a common is that they share a deep understanding of a specific category and what it takes to demonstrate and deliver clinical value that is worth paying for.

PII Methodology

Hypothesis:
If two companies each had the same NCE at the same stage of development (say end of phase I), which company would do the best job of commercialising the product?
i.e., which company adds most in the strategic sense (but not tactical., e.g. number of reps, details delivered, etc).

Constraints:
Cannot measure directly, therefore need to deploy surrogate measures.
Each measure or index must exist (somewhere), be gettable (either full or derivable), be useable (compare like with like, transferable).

Indices identified to date to rank Top 30 pharma include:
1. Global sales/ market capitalisation – a measure of the funding available for commercialisation efforts:
   a. Trend in historical sales and share movements
   b. Projected/ analyst forecast sales and share movements
2. Regulatory efficiency: Speed to market, end-of-phase I to launch, regulatory success ratio, etc.
3. Attrition rate in phase III - particularly failure on efficacy grounds vs placebo or standard of care
4. Value proposition, need for product:
   a. Did products achieve reimbursement, NICE approval?
   b. Did FDA grant expedited processing or breakthrough status?
   c. Developing first in class NCEs or novel mechanisms of action
5. Sales vs ostensibly similar molecule; relative ranking
6. Gearing, sales and marketing spend vs turnover
7. Ratio of new product ideas vs 'me-toos'
8. 'Freshness index' - percentage of company sales generated by products launched in the last three to five years
9. Analyst ranking

In addition, IDEA Pharma monitors company web sites, annual reports and industry sites to identify single or short-term events that would increase or decrease a company's PII ranking, e.g.
1. Changes in R&D strategy, research collaborations
2. Company restructuring to capitalise on areas of strength, optimisation of portfolios/ franchises
3. Innovative commercialisation or sales strategies (including social media)

Each of the above are collated by company and weighted to produce the PII.