Evaluate Vantage

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Failure to launch for last year's big hopes

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Back in the comparatively financially buoyant days of January 2008, EP Vantage compiled a list of the biggest product launches, in terms of future sales potential, as forecast by financial analysts for the coming 12 months. (*Which of this year's launches will be future blockbusters? January 4, 2008*). Revisiting those candidates and their progress does not make happy reading.

Of the 20 biotech and conventional drugs identified, only 7 have managed to make it to the market, although Actemra and Stelara have very recently won approval and should be launched in the very near future. This lack of progress has eroded 39% or $6.65bn from combined 2012 sales forecasts for those products (see table). It would appear that 12 months ago even in the face of increasingly burdensome regulatory demands financial analysts were maintaining a sense of optimism that was rarely borne out by reality. Whether the delays of last year will prompt exuberant forecasters to show some restraint remains to be seen.

The number of products that won approval in the US, the world’s most important drug market, is even more disappointing, with only five winning FDA backing. It should be noted that Boehringer Ingelheim’s Pradaxa has not yet sought a license in the US.

The significant difference between expectations among the analyst community and what actually happened could in part be explained by big hold ups at the FDA over the year, due to a lack of resources, which took many by surprise. This could also explain why only one drug, Pristiq, saw any upgrades over the year, although again unrealistic forecasting is likely to have played a part.

Also, looking at the list of products, many realistically should not have been considered potential 2008 launches, such as the cancer vaccines and gene therapies. However, drugs like Merck & Co’s Cordaptive, a small molecule drug with a regulatory pathway that should have been easier to forecast, was derailed.

Still, forecasts are only that, predictions that come with major caveats. However, with regulators holding up even seemingly straight forward drug approvals, it seems that a more pessimistic approach might yield more accurate figures.

Biggest selling products forecast to launch in 2008 ($m)							
	Rank	**Product**	**Company**	**2012 sales forecast in January 08**	**Current 2012 sales forecast**	**Phase at Jan 2008**	**Current phase**
Biotechnology	1	Actemra	Roche	2,249	1,555	Filed	Approved*
	2	Stelara	Johnson & Johnson	995	721	Filed	Approved*
	3	Simponi	Johnson & Johnson/Schering Plough	1,546	1,516	Phase III	Filed
	4	Synflorix	GlaxoSmithKline	821	389	Phase III	Filed
	5	CP-675,206	Pfizer	555	6	Phase III	Phase II
	6	MDX-010	Bristol-Myers Squibb	481	180	Phase III	Phase III
	7	SpecifId	Favrille	445	0	Phase III	Abandoned
	8	Recothrom	ZymoGenetics/Bayer	352	261	Filed	Marketed
	9	Advexin Therapy	Introgen Therapeutics	202	0	Filed	Filed/suspended
	10	Cerepro	Ark Therapeutics	178	139	Phase III	Filed*
Total				**7,825**	**4,767**		
Conventional	1	Pradaxa	Boehringer Ingelheim	1,319	1,281	Filed	Marketed
	2	Paliperidone palmitate	Johnson & Johnson	1,126	507	Filed	Filed
	3	Effient	Eli Lilly	1,078	900	Phase III	Filed
	4	Zevtera	Johnson & Johnson	939	561	Filed	Marketed*
	5	Tredaptive	Merck & Co	872	205	Filed	Marketed*
	6	Relistor	Wyeth	865	411	Filed	Marketed
	7	Vimpat	UCB	742	425	Filed	Marketed
	8	Viviant	Wyeth	735	153	Filed	Filed
	9	Onglyza	Bristol-Myers Squibb	726	315	Phase III	Filed
	10	Pristiq	Wyeth	627	676	Phase III	Marketed
Total				**9,029**	**5,434**		
Grand Total				**16,854**	**10,201**		

Product updates

Roche's **Actemra** won approval in Switzerland and in Europe last month, but a green light in the all important US market is still eluding the company. A request for further pre-clinical studies and a Risk Evaluation and Mitigation Strategy (REMS) from the FDA last December means a resubmission is anticipated in the third quarter of this year, meaning a launch in the US does not look likely until 2010. (*Delay to Roche's Actemra robs 2008 of its biggestapproval,* December 04, 2008.)

Johnson & Johnson's ustekinumab, now branded **Stelara**, was approved in Canada in December, but received a complete response letter from the FDA the same month and was granted a marketing license in Europe in January. The US regulator against asked for a Risk Evaluation and Mitigation Strategy (REMS) to be set out, but no other further trials. J&J is expected to re-file any time now, meaning approval this year looks likely. This means that whilst forecasts have gone down for 2012, they have probably just been discounted for a year's delay.

Also for J&J, golimumab, branded **Simponi**, has been filed in the US and has a PDUFA date of April 27, whilst a decision from Europe regulators is expected in the first half of the year.

Synflorix forecasts have come down significantly, and yesterday Glaxo's chief executive, Andrew Witty, confirmed that the vaccine will probably not be launched in the US. The decision is based on the prevalence of certain pneumococcal subtypes. In Europe the drug was recommended for approval last month.

CP-675,206 is a notable failure. Pfizer scrapped phase III trials of the melanoma treatment in April, after interim data suggested that the drug was no better than standard chemotherapy, although earlier studies in a range of solid tumours are ongoing. (*Pfizer's melanoma disappointment compounds Medarex misery*, April 02, 2008)

Ipilimumab also suffered a setback when the FDA asked to see additional survival data, delaying and potential approval by two years. Data due later this year is keenly awaited. (*Confidence in Medarex's ipilimumab dented again, April 28*, 2008).

Favrille's **Specifid** was one of a number of cancer vaccine failures last year. (*Favrille failure puts pressure on other cancer vaccines, May 28, 2008*)

Introgen found itself in dire straights after the FDA refused to even review **Advexin**, a gene therapy cancer treatment. (*Introgen's FDA rebuff could prove fatal*, September 03, 2008) The group has recently filed for chapter 11 bankruptcy protection and accepted the resignation of its entire management board, meaning the product is highly unlikely to reach the market any time soon.

Ark Therapeutics' gene therapy **Cerepro**, for brain cancer, has now been filed in Europe. Considering the high unmet need for treatments for high grade glioma, approval this year might be possible, but like Introgen's Advexin, the extremely novel approach makes it a high risk project.

Zymogenetics **Recothrom**might be one of the few potential launches of last year to actually make it, but takeup has been a big disappointment, hence the downgrade to 2012 sales consensus. (*ZymoGenetics' Recothrom set to be one of the most disappointing new product launches of 2008*, November 05, 2008).

Boehringer Ingleheim's anti clot drug **Pradaxa** won approval in Europe in April, but has seen downgrades since, possibly after a rival new drug, Xarelto from Bayer, won approval later in the year.

In August, the FDA issued a complete response letter to J&J and asked for further information on the antipsychotic **paliperidone palmitate**, hence the downgrade to 2012 forecasts, the company responded to the regulator today.

Only this week an FDA advisory committee recommended approval to Eli Lilly's **Effient**, although delays throughout the year meant forecasts were pushed out. (*FDA panel removes another hurdle for Effient approval,*February 04, 2009)

Despite winning approval in Switzerland and a positive recommendation in Europe, antibiotic **Zevtera** has struggled to past muster with the FDA, with some analysts fearing a marketing license not be granted for at least another 12 months.

Merck & Co's heart drug **Tredaptive** has been approved in Europe, but once again US regulators threw a spanner in the works, handing the drug a non-approvable letter. The group is now going to have to wait for the results of an ongoing outcomes study, expected to be completed in early 2013, before it can re-file; a significant delay, hence the downgrades.

Wyeth's **Relistor** finally won approval in April, after a delay which caused forecasts to be pushed back, whilst disappointing sales figures since launch have caused further downgrades to what looked like highly optimistic projections. (*Progenics needs the tide to turn on Relistor,* October 24, 2008)

UCB's **Vimpat** finally won approval in the US in October for adult seizures, but the potential of the drug has been damaged by the drug's failure to win a green light in diabetic neuropathic pain. (*UCB finally has something to celebrate*, October 29, 2008)

A third approvable letter for Wyeth's osteoporosis drug **Viviant** in May took its rejection tally up to three, and the company is still compiling its response for the regulator, causing forecasts to significantly plunge over the year.

DPP-IV diabetes treatment **Onglyza**, being developed by Bristol-Myers Squibb and AstraZeneca, has been filed and is awaiting a decision in the US by April 30, and in Europe later this year. Forecasts have come down gradually over the year as it has become increasingly apparent that taking market share from Merck & Co's Januvia, the first DPP-IV to reach the market, is going to be tough.

Lastly, Wyeth's depression pill **Pristiq** won US approval in February, and generated sales of $67m last year, the company revealed last month. However, failure to win approval in Europe has probably capped any upgrades.