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BIGGEST LAUNCHES 2014

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The recent staggering performance of the biotech industry has been built around a belief that the sector's R&D productivity is on the rebound and will deliver huge investor returns in the coming years. But a look at the forecast launches for 2014 tells a more modest tale.

Only three drugs slated to be launched this year will achieve blockbuster status by 2018, according to EvaluatePharma's consensus, a disappointing projection considering at least six blockbusters-in-waiting reached the market every year for the last four. Not all of these reached this billion dollar threshold, of course – for example, 2010 saw the launch of the spectacular disappointment Provenge. But today's comparatively sedate view of the potential of coming launches makes a stark counterpoint to the stock market's exuberance.

The industry's move towards so-called "nichebuster" drugs could help explain some of the migration, and these drugs are often in the orphan indications that deliver greater return on investment than their primary-care counterparts. And 2013 saw the launch of 10 new molecules forecast to become future blockbusters, including Gilead's Sovaldi and Biogen Idec's Tecfidera – a stand-out year for future earnings potential. Yet billion-dollar drugs remain an indicator of the sector's productivity, and their absence in the 2014 launch class is an indicator that should be watched closely.

Biggest Expected Launches of 2014

						Annual WW Sales ($m)	
		Product	Company	Status	Therapeutic Area	2014	2018
Biotechnology	1	RLX030 (serelaxin)	Novartis	Filed	Heart failure	100	903
	2	Dulaglutide	Eli Lilly	Filed	Anti-diabetic	102	835
	3	Afrezza	MannKind	Filed	Anti-diabetic	51	725
	4	Eloctate	Biogen Idec/Swedish Orphan Biovitrum	Filed	Clotting factor	41	692
	5	IMC-1121B (ramucirumab)	Eli Lilly	Filed	Cancer antibody	37	684
	6	LY2963016	Eli Lilly	Filed	Anti-diabetic	10	649
	7	AIN457 (secukinumab)	Novartis	Filed	Psorasis	32	572
	8	V503	Merck & Co	Phase III	HPV vaccine	51	521
	9	Plegridy (peginterferon beta-1a)	Biogen Idec	Filed	MS therapy	53	504
	10	ENB-0040	Alexion Pharmaceuticals	Phase III	Enzyme replacement therapy	4	467
Total Biotech Products						*481*	*6,552*
Conventional	1	Anoro Ellipta	GlaxoSmithKline	Approved	COPD therapy	231	1,740
	2	Brintellix	Takeda/Lundbeck	Approved	Anti-depressant	271	1,435
	3	Apremilast	Celgene	Filed	Rheumatoid arthritis therapy	93	1,219
	4	Empagliflozin	Boehringer Ingelheim	Filed	Anti-diabetic	86	769
	5	Idelalisib	Gilead Sciences	Filed	Cancer kinase inhibitor	26	528
	6	CXA-201 (ceftolozane, tazobactam)	Cubist Pharmaceuticals	Phase III	Antibiotic	4	473
	7	Omidria (OM302)	Omeros	Filed	Eye therapy	29	452
	8	Contrave	Takeda	Filed	Anti-obesity agent	24	395
	9	Zerenex	Keryx Biopharmaceuticals	Filed	Phosphate binder	32	392
	10	Tavaborole	Anacor Pharmaceuticals	Filed	Anti-fungal agent	13	381
Total Conventional Products						*808*	*7,783*
Launches that could happen in 2014							
Biotechnology	1	Nivolumab	Bristol-Myers Squibb/Ono Pharmaceutical	Phase III	Cancer antibody	-	3,922
Biotechnology	2	MK-3475 (lambrolizumab)	Merck & Co	Phase III	Cancer antibody	-	1,646
Total						-	*5,568*

Source: EvaluatePharma ©2014

The above table was constructed from consensus data from EvaluatePharma, to find the biggest forecast launches of the year, as projected by equity analysts.

Of course, the picture could change remarkably should the anti-programmed death-1 (PD-1) antibodies manage to launch this year. Merck's surprise announcement this month that it had started a rolling submission for MK-3475 means if all goes well regulators could give the product a green light before the year is out. Given the huge potential and intense competition in this space, the company will no doubt be ready to launch as soon as possible.

Bristol-Myers Squibb's nivolumab is not far behind, and it could file its PD-1 contender in third-line squamous non-small cell lung cancer this year as well; Merck's filing will be in melanoma patients refractory to Yervoy. Even if these launches do not happen until 2015 the progress of these agents will have been remarkable. And with huge commercial as well as clinical potential seen, they will likely represent substantial launches in whatever year they debut.

On Track for Take Off

More certain to become the blockbusters of 2014 are GlaxoSmithKline's combination COPD therapy Anoro Ellipta, Lundbeck's Brintellix and Celgene's psoriatic arthritis drug apremilast.

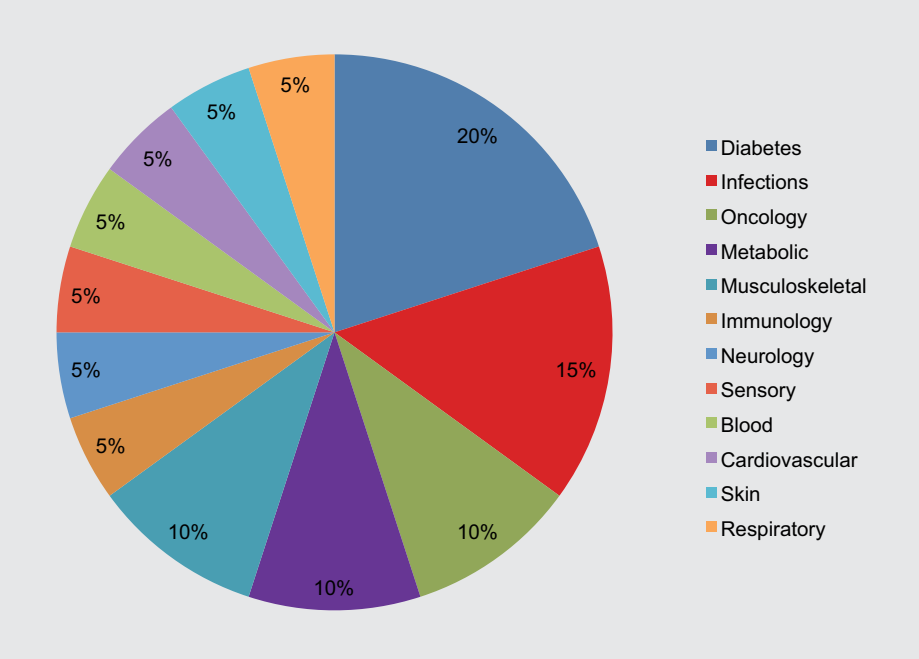
Anoro is a long-awaited COPD drug and part of a new wave of combination long-acting beta 2 adrenoreceptor agonist (LABA) & long-acting muscarinic antagonist (LAMA) drugs to hit the market in coming years. It received US approval in December and Glaxo expects to launch it in the first quarter of 2014.

Takeda and Lundbeck launched Brintellix in January; the novel inhibitor of serotonin reuptake has been approved in both the US and Europe for major depressive disorder, a poorly treated illness. As such, the product is thought to have considerable potential.

Apremilast would be the second new anti-rheumatic to hit the market in two years – after Pfizer's Xeljanz – but would be playing initially in the psoriatic arthritis space. Its blockbuster forecast depends on getting approval in psoriasis, an indication for which it has yet to be filed with regulatory authorities. Celgene recently reiterated its sales guidance of $1.5-$2bn for the product by 2017, but not all forecasters believe that the product will be taken up this quickly.

Novartis' RLX030, known variously as serelaxin or relaxin, comes tantalisingly close to a blockbuster forecast, with $903m in sales expected in 2018. There is a great deal of uncertainty about whether this intravenous medication will be launched this year; it is a recombinant form of a natural hormone that becomes elevated during pregnancy that Novartis has developed as a treatment for acute heart failure. A negative opinion from European regulators in January did not come as a huge surprise considering that trial data had been equivocal about its efficacy. However, the project has earned FDA breakthrough therapy designation, so the US agency might be favourably inclined to approval.

Biggest Launches of 2014 By Therapy Area



Source: EvaluatePharma ©2014

It is not too surprising to see cancer drugs well represented in the list of this year's big launches given the R&D priorities of big pharma and biotech alike – three make the list, with Eli Lilly's ramucirumab and Gilead Sciences' idelalisib joining nivolumab. A little more surprising, given the high cost and scale of clinical trials to get them to market, is the presence of four diabetes drugs, making treatments for endocrine-related disorders the biggest category of products forecast for launch.

Eli Lilly's dulaglutide and empagliflozin, the latter of which is partnered with Boehringer Ingelheim, look like they have a decent shot at approval. The competitive position of the former will be judged on its performance against Victoza, which is the leader of the GLP-1 class and against which similar agents have proved inferior. Success for dulaglutide in its head-to-head test against Victoza could have analysts reassessing their view of its sales potential.

Lilly's insulin glargine LY2963016, a biosimilar to Sanofi's Lantus, also makes the list of top launches. However a seemingly unanticipated patent infringement lawsuit launched by the French drug maker this month looks certain to result in a stay of the FDA's hand, keeping the Lilly copycat off the market until at least 2016.

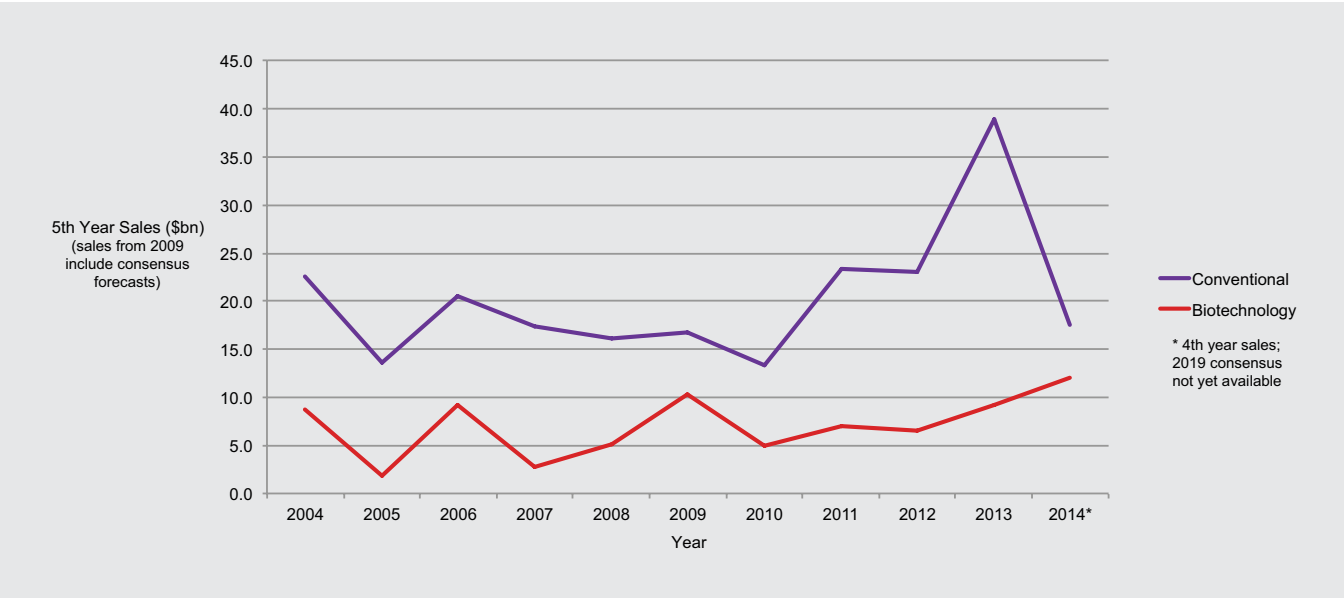
The fourth anti-diabetes project, Afrezza, is an extremely high-risk bet; the project has its share of detractors as well as supporters, and the consensus forecast here will represent a best-case scenario. The inhaled insulin has been rejected twice by the FDA, and, even if it does pass regulatory muster, achieving the current sales forecast of $725m will be a tall order.

Another category that tops the list, somewhat counterintuitively, is anti-infectives. A great deal of worry has been expressed about the future of antibiotics given the rise of resistance, and the industry has not been especially quick to respond. However, the possibility that Cubist Pharmaceuticals' CXA-201, a treatment for hospital-acquired infections from Gram-negative bacteria, could soon be on the market should be received with some applause. Whether it makes it to market this year remains

to be seen – although the company has committed to filing in the first half of the year and the product has fast track status, a launch in 2014 would represent swift progress.

At forecast 2018 sales of $473m, CXA-201 will be nipping at the heels of the leading infection-related product, Merck & Co's human papillomavirus (HPV) vaccine V503. It is hoped that this nonavalent vaccine – offering protection from five more strains of HPV than the market leader, Merck's blockbuster Gardasil – will present a better pharmacoeconomic argument as it shields women from the strains that cause 90% of cervical cancers, versus Gardasil's 70%.

5th Year Sales of All Launches Per Year



Source: EvaluatePharma ©2014

The chart above shows the combined fifth-year sales for all products launched each year over the last decade, for which companies and analysts provide data. From 2009 the data include increasing proportions of consensus forecasts.

It also shows that, despite the growing importance of biologics and the industry's increasing focus on the technology, small molecules still dominate new medicines.

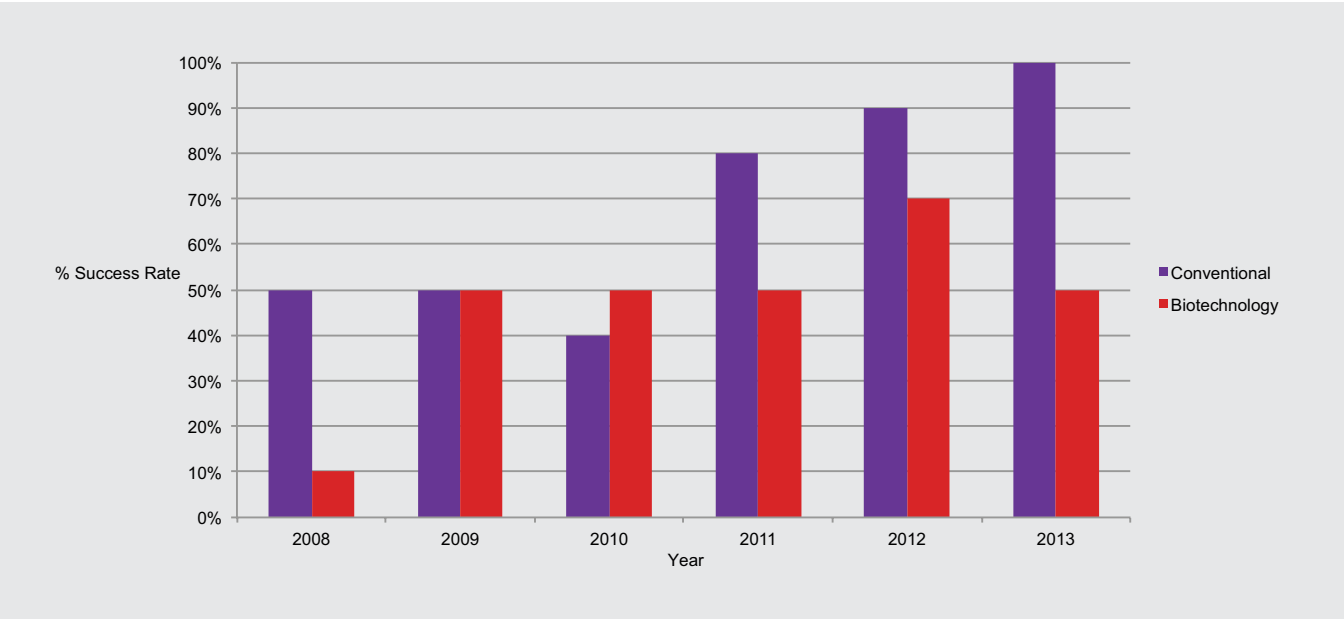
However, if these forecasts prove accurate 2014 could be one of the best years for launches of biological products. If the PD-1 antibodies make it, it will look even better.

The graph reveals how over the past 10 years the value of new biologic launches has been trending upwards. Launches of conventional pharma products, on the other hand, show bigger oscillations but reveal no trend towards greater sales, the successful class of 2013 notwithstanding.

These graphs also reveal how dependent the industry is on launching giant new products to restore faith in the sector's R&D productivity. The dip in the value of conventional products launched from 2006 to 2010 helped stoke concerns about the industry's ability to invent substantial new drugs and coincided with worries over the "patent cliff". This productivity image problem was not helped by a string of late-stage disappointments and delays that befell a number of products pegged as future blockbusters.

However, the analysis below shows how the regulatory process has become more predictable. This was constructed by taking the 10 biggest biological or conventional products projected to launch each year, and tracking their progress in reaching the market in either the US or Europe. It found that in 2008 only 50% of the small-molecule products and 10% of the biologicals forecast to reach the market that year actually made it. In 2013 that number had improved to 100% in the conventional pharma camp and 50% in biologicals.

Percentage of Projected Top Ten Launches That Made it to Market on Time



Source: EvaluatePharma ©2014

This analysis is not a measure of first-pass approvals – some products that failed to win a marketing licence at the first attempt were still attracting substantial forecasts as they approached a second hearing, and as such may appear in a subsequent year's analysis.

But, even with these caveats, it supports the thesis that regulatory action is becoming more predictable and timely. An interesting inflection occurs in 2011, which coincides with the FDA's implementation of new rules and procedures under the Food and Drug Administration Safety and Innovation Act, commonly known as PDUFA V. One of the aims of this law was to enhance communications between the agency and sponsors to increase the number of first-cycle approvals.

It also suggests that pharma and biotech companies are getting better at killing unpromising projects as interactions with the FDA reveal more about the size and scope of data that will be necessary to support approval. This "failing faster" approach has been advocated by many in the sector as a way of reducing clinical trial costs and restoring confidence that the R&D machine can improve productivity.

Meeting Launch Expectations

This improvement in the industry's launch-on-time record was on display last year. Not only were most biologics and all conventional products on the market when forecast, but three were available earlier than expected.

At the beginning of 2013 Gilead's hepatitis C pill Sovaldi was considered a 2014 launch, but swift progress and strong data saw it win approval in December, and the company wasted no time opening the factory gates. Expectations have surged as well, by a remarkable 38% in the past 12 months to $7.4bn for 2018.

Both Imbruvica and Gazyva benefited from the FDA's breakthrough therapy designation status and won much earlier approvals than expected, making these cancer therapies 2013 launches.

Elsewhere, the launch timetable for 2013 performed as expected across the year, and it is notable that several products attracted big sales forecast upgrades across the year.

Roche's antibody drug conjugate Kadcyla saw its 2018 forecast more than doubled to $3.6bn. Expectations were huge for Tecfidera, Biogen Idec's powerful multiple sclerosis pill, and yet the forecast for this drug still inflated over the year by 35% to $5.1bn.

Progress of Biggest Products Forecast to Have Launched in 2013

Biotechnology	Rank	Product	Company	Therapeutic Area	Status 2013	Current Status	2018 Sales Consensus in Jan 2013 ($m)	Current 2018 Sales Consensus ($m)	Change
	1	Kadcyla (trastuzumab-DM1)	Roche	Cancer antibody drug conjugate	Filed	Marketed	1,402	3,565	154%
	2	Heplisav	Dynavax Technologies/ Undisclosed Partner Sales	Hepatitis B vaccine	Filed	Filed	592	150	-75%
	3	Vimizim (GALNS)	BioMarin Pharmaceutical	Enzyme replacement therapy	Phase III	Filed	503	458	-9%
	4	V503	Merck & Co	HPV vaccine	Phase III	Phase III	458	521	14%
	5	NovoEight (turoctocog alfa)	Novo Nordisk	Clotting factor	Filed	Approved	395	257	-35%
	6	Kynamro	Sanofi	Anti-hyperlipidaemics	Filed	Marketed	344	379	10%
	7	Lemtrada	Sanofi	MS therapy	Filed	Marketed	340	619	82%
	8	Eperzan (albiglutide)	GlaxoSmithKline	Anti-diabetic	Phase III	Filed	327	416	27%
Total Biotech products							*4,362*	*6,365*	*46%*
Conventional	1	Tecfidera (BG-12)	Biogen Idec	MS therapy	Filed	Marketed	3,746	5,053	35%
	2	Tivicay (dolutegravir)	GlaxoSmithKline	HIV therapy	Filed	Marketed	1,359	2,124	56%
	3	Olysio (simeprevir)	Johnson & Johnson	Hepatitis C treatment	Phase III	Marketed	1,248	482	-61%
	4	Breo Ellipta	GlaxoSmithKline	COPD therapy	Filed	Marketed	1,208	1,885	56%
	5	Xofigo (alpharadin)	Bayer	Cancer radiotherapy	Filed	Marketed	1,113	1,210	9%
	6	Ultibro Breezhaler (QVA149)	Novartis	COPD therapy	Filed	Marketed	1,015	979	-4%
	7	Abilify Maintena (Abilify Depot)	Otsuka Holdings	Schizophrenia treatment	Filed	Marketed	944	1,240	31%
	8	Adempas (riociguat)	Bayer	Pulmonary hypertension treatment	Phase III	Marketed	937	803	-14%
	9	Invokana	Johnson & Johnson/Mitsubishi Tanabe Pharma	Anti-diabetic	Filed	Marketed	918	1,096	19%
	10	Opsumit	Actelion	Pulmonary hypertension treatment	Filed	Marketed	836	1,086	30%
Total Conventional products							*13,324*	*15,958*	*20%*
Earlier Than Expected Significant Launches									
Conventional	1	Sovaldi	Gilead Sciences	Hepatitis C treatment	Phase III	Marketed	5,340	7,363	38%
Conventional	2	Imbruvica	Pharmacyclics	Cancer kinase inhibitor	Phase III	Marketed	2,480	1,850	-25%
Biotechnology	3	Gazyva	Roche	Cancer antibody	Phase III	Marketed	451	905	101%
Total							*8,271*	*10,118*	*22%*

Source: EvaluatePharma ©2014

Growing hopes for these products no doubt reflects the enthusiasm for the biotechnology sector that was apparent in share prices across 2013 – and probably helped fuel that optimism as well.

Of course not all prospects improved – a call from the FDA for further studies of Dynavax's hepatitis B vaccine Heplisav caused expectations to tumble, and the runaway success of Sovaldi has harmed the prospects for Johnson & Johnson's Olysio (simeprevir).

But, in spite of these slips, if the class of 2013 meets current expectations it will include an incredible 10 blockbuster drugs by 2018, with another two not far behind. This will be a difficult act to follow, and the class of 2014 is not shaping up to match these numbers. How this affects investors' views of the biotech sector will be one of the interesting stories of the year.

Report author: Jonathan Gardner

EDITORIAL TEAM

Lisa Urquhart
Editor
LisaU@epvantage.com
@LisaEPVantage

Amy Brown
Senior Reporter
AmyB@epvantage.com
@AmyEPVantage

Jonathan Gardner
Reporter
JonathanG@epvantage.com
@JonEPVantage

Jacob Plieth
Senior Editorial Analyst
JacobP@epvantage.com
@JacobEPVantage

Elizabeth Cairns
Medtech Reporter
ElizabethC@epvantage.com
@LizEPVantage

Joanne Fagg
Editorial Assistant
JoanneF@epvantage.com
@JoEPVantage

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FOR GENERAL QUESTIONS
ON THIS REPORT, CONTACT

Christine Lindgren
Vice President, Marketing
Christine.Lindgren@evaluategroup.com
+1 617 573 9458

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Evaluate – Headquarters – Evaluate Ltd., 11-29 Fashion Street, London E1 6PX United Kingdom
Tel: +44 (0)20 7377 0800 – Fax: +44 (0)20 7539 1801

Evaluate – North America – EvaluatePharma USA, Inc., 15 Broad Street, Suite 401, Boston, MA 02109 USA
Tel: 1-617 573-9450 – Fax: 1-617 573-9542

Evaluate – Japan – EvaluatePharma Japan KK, Tokyo, Japan
Tel: +81 (0) 80 1164 4754

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