

The mega-blockbusters - biologicals dominate biopharma's hall of fame



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By the end of 2017 six prescription medicines had achieved lifetime sales in excess of \$100bn, a figure that Ecuador would be proud to generate in annual GDP. Lipitor, Humira and Epogen occupy the top spots; kudos to those who can name the other three.

If sales forecasts hold, a further four products could join this illustrious club by the end of 2022, according to *EvaluatePharma*. It is notable that this group is dominated by biologicals, which particularly in the US have benefited from huge pricing power and lengthy market exclusivity that their small-molecule cousins could only dream of. But, if remarks by US FDA commissioner Scott Gottlieb this week are anything to go by, pressure is growing to dismantle these benefits (see tables below).

In a [speech](#) to America's Health Insurance Plans' annual conference yesterday Mr Gottlieb pulled no punches in calling out practices that he believes are holding back the US's nascent biosimilar space. That the US has lagged Europe in its embrace of biosimilars is no secret, and has been helped by the huge sums that originators have thrown at intellectual property defence, nervousness among physicians and delays in establishing regulatory pathways.

While promising to improve the agency's efforts in nurturing the biosimilars industry, Mr Gottlieb took the opportunity to point a finger at rebate and contracting practices. As he described it these arrangements between pharmacy benefit managers, insurers and manufacturers effectively rig the system, diminishing the financial incentive for biosimilars developers.

He is not the first to notice this. Pfizer's lawsuit alleging that Johnson & Johnson was using uncompetitive contracts to protect its Remicade franchise in the US alludes to the same issue ([For US traction, biosimilars makers must get the payers on side](#), 1 November 2017). Remicade stands as one of the most commercially successful drugs to date, a record that in later years has been bolstered by delays to competition in the US.

Biopharma's mega-blockbusters - the biggest drugs to date

Product	Primary company	Cumulative global sales to 2017 (\$bn)	First global launch	Years of market exclusivity
Lipitor	Pfizer	162.2	1997	14
Humira	Abbvie	116.1	2003	20
Epogen	Amgen/J&J	105.9	1998	20**
Rituxan	Roche	104.6	1997	21**
Advair	Glaxosmithkline	100.9	1998	18
Enbrel	Amgen/Pfizer	100.7	1998	30**
Zantac	Glaxosmithkline	95.1*	1981	16
Remicade	J&J	92.0	1998	18
Plavix	Sanofi/Bristol-Myers Squibb	88.9	1998	14
Herceptin	Roche	80.8	1998	21**

*Note: Sales include those reported by global partners; *total will be higher as sales pre-1986 are unavailable; **still under litigation, based on estimates for patent expiry in the US. Source: EvaluatePharma.*

Of course the "rebate trap" that Mr Gottlieb described is only one factor that has helped biological products achieve such eye-watering lifetime sales. All also delivered significant clinical advances, and many won approval across several indications. For example the anti-TNF agents - Humira, Remicade and Enbrel - are approved in a broad

spectrum of auto-immune conditions.

But the analysis above does illustrate how monoclonal antibodies and recombinant proteins have, typically, enjoyed substantially longer market exclusivity than small molecules. Partly this reflects greater complexity, an argument also used for charging substantially higher prices than for conventional medicines, another reason for biologicals' commercial greatness.

It is also notable that biologicals' dominance is only set to grow in this analysis – if sales forecasts out to 2022 are included only three small molecules remain in the top 10: Lipitor, Advair and Revlimid.

Biopharma's mega-blockbusters - including forecasts to 2022		
Product	Primary company	Cumulative global sales to 2022 (\$bn)
Humira	Abbvie	223.7
Lipitor	Pfizer	171.5
Enbrel	Amgen/Pfizer	132.0
Rituxan	Roche	128.7
Remicade	J&J	115.6
Epogen	Amgen	112.9
Advair	Glaxosmithkline	112.1
Avastin	Roche	107.3
Herceptin	Roche	106.0
Revlimid	Celgene	102.9

Note: Sales includes those reported by global marketing partners. Source: EvaluatePharma.

It should be noted that a couple of the products above are awaiting pivotal decisions that will help determine future sales.

Glaxo's respiratory giant Advair is one: its patents have already expired, but US approval of substitutable generics is stalled, putting future sales in this region in the hands of the FDA. And Enbrel could yet prove the poster child for patent life; Amgen is defending US intellectual property stretching out for another decade that, if upheld, would grant a gluttonous stretch of market exclusivity.

Every extra hour of patent life helps, as Abbvie demonstrated when it managed to delay biosimilar threats to Humira for longer than many presumed possible ([Abbvie sets the date for cash cow slaughter, 28 September 2017](#)).

These extra months will help Humira grab Lipitor's crown as the most commercially successful drug by 2020 – Abbvie's monster product is forecast to generate \$14bn in sales in the US in each of the next five years. As an aside, the fact that Lipitor managed to achieve its record with only 14 years of patent protection is telling of this brand's power.

Much to do

Humira is also remarkable for the fact that it still has so much to do. As the analysis below shows, projected sales over the next five years almost equal its historic record.

Revlimid looks similar in this regard, spelling out how the fortunes of the blood cancer drug remain so pivotal to Celgene, as does Prevnar 13, a hugely successful vaccine that is responsible for Pfizer's place in this league. The appearance of the most recent launches in this analysis, the immuno-oncology agents Keytruda and Opdivo, highlight how revolutionary these drugs are considered.

Of course owning those with the most to do implies huge pressure to deliver – though most companies would consider this a nice problem to have. But Mr Gottlieb's intervention this week is only one sign that amassing such huge franchises is going to get harder as the US wakes up to its status as the world's most profligate healthcare spender.

Not that change is expected to happen fast, if Enbrel's presence in the list below is anything to go by. If a product launched 20 years ago can still be considered one of the most lucrative global franchises in the coming years, efforts in the US to increase competition and control drug prices have a long way to go.

Those with most to do - top cumulative sales 2018-22

Product	Primary company	Forecast sales 2018-22 (\$bn)	Cumulative global sales to 2017 (\$bn)	First global launch
Humira	Abbvie	107.6	116.1	2003
Revlimid	Celgene	59.0	43.9	2006
Keytruda	Merck & Co	42.6	5.9	2014
Xarelto	Bayer/J&J	40.0	20.7	2008
Opdivo	Bristol-Myers Squibb	39.0	11.6	2014
Eylea	Regeneron/Bayer	35.3	22.1	2011
Enbrel	Amgen/Pfizer	31.2	100.7	1998
Imbruvica	Abbvie/J&J	31.1	7.3	2013
Prevnar 13	Pfizer	28.3	37.3	2009
Avastin	Roche	27.2	80.1	2004

Note: Sales includes those reported by global marketing partners. Source: EvaluatePharma.

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