



Biosimilars: Market Changes Do Not Equal Policy Success

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Background

In our April 2019 report “[Biologics Are Natural Monopolies](#),” we characterized the market for biologic drugs as one of “natural monopoly,” a result of “intrinsic scientific uncertainties that make creating interchangeable substitutes difficult, costly, slow and risky.” At that time, nine years after the passage of the [Biologics Price Competition and Innovation Act](#) (BPCIA), we showed that biosimilar entry was spotty and price declines following entry were modest.

Few biologics that were due to face competition actually did. Of those, the number of competitors was meager. Even when there was more than one competitor, price declines were slow in pace and slight in magnitude when compared to what is seen when small molecule drugs face generic competition. We argued that policymakers should [explore an alternative approach](#) to reducing prices of biologic drugs after their monopoly period had finished. At that time, the innovator companies should lower their prices to equal the costs of production (including facility repair and replacement) and market distribution, plus an appropriate profit; we have named this approach [Production Plus Profit Pricing](#) (or P-quad).

But since the time of our report nearly two years ago, numerous articles and analysts’ research reports have trumpeted biosimilar market growth, suggesting that the skeptics (including us) had been wrong. They have cited rising sales as evidence that biosimilars are no longer an experiment destined to fail. Some recent catchy headlines tell the story: “Biosimilars have arrived on the US shores”¹ and “[Pfizer, Amgen will rake in billions in ‘golden age’ for biosimilars](#).” The biosimilars market according to some reports has in fact tripled in size from the time we published our assessment. By the end of 2020 it was annualizing at \$3.9 bn, compared to \$1.2 bn based on 2Q19.²

It’s crucial that policymakers keep sight of the sole objective for creating the biosimilar pathway: to [reduce the cost of older biologic drugs](#) for society and taxpayers immediately following a designated period of market exclusivity and monopoly pricing power. Biosimilars should achieve the same ultimate goal as generic drugs and reduce the price of branded medicines when their exclusivity ends. By choosing biosimilar entry as a means to achieve that end, policymakers are betting that strong and rapid competitive pressure from biosimilars will result in substantial price reductions by both innovator company and biosimilar competitors, or at least that nearly all volume will shift to that low competitive price.

Put another way, policymakers should be wary of assuming that biosimilar entry and market penetration are adequate surrogate markers of the approach’s success. Policymakers should be asking if biosimilars are challenging every biologic drug that has reached its end of exclusivity (or nearly so), and whether that competitive pressure is meaningfully driving

¹ Aaron (Ronny) Gal, Ph.D. “Biopharma Weekly (8/3/20),” Sanford Bernstein, August 3, 2020

² Aaron (Ronny) Gal, Ph.D., “Biosimilars (Dec. Update),” Sanford Bernstein, December 15, 2020

down net prices for both the innovator and its competing biosimilars (the average of the innovator and biosimilar prices weighted for market share).

Today's biosimilar market evinces neither of these features. Rather, the good fortune, literally, for biosimilar manufacturers is predominantly a product of high prices, captured by mildly competing against only a handful of the largest biologic drugs. In this paper we examine the available data regarding the biosimilar market in the US over the two years since we published our assessment.

Do All Eligible Branded Biologics Face Competition?

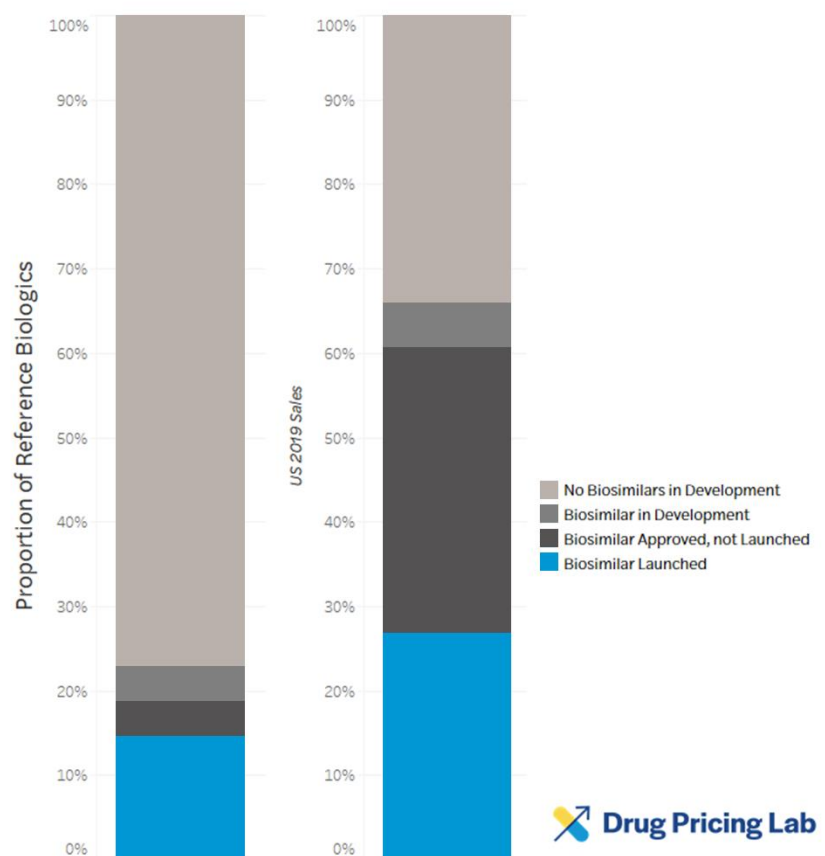
Eligible post-exclusivity biologics must face competition, but most aren't (and likely won't)

That some biologic drugs face competition is not evidence that all do (or will); however, for biosimilar policy to produce the desired savings ubiquitous competition is needed. Today, few of the biologics that are past their loss of exclusivity date face biosimilar competition -- or even the

prospect of it. As of the end of 2020, seven reference biologic drugs are facing competition (from 18 biosimilars). That amounts to only 15% of all biologic drugs that were past exclusivity facing any competition, a sub-group that collectively accounts for only [27% of revenues](#) earned by post-exclusivity biologics (based on 2019 US revenues) (Figure). The market will not stay like this over the next decade, but it isn't likely to improve that much either, with the exceptions of the expected entries of already approved biosimilars for Enbrel ([as late as 2029](#)) and Humira ([expected in 2023](#)).

According to a [recent report by IOVIA](#), only 22 additional molecules have biosimilars in development, whereas 153 reference biologics do not yet have any in development. Many of these products are for rare diseases and do not have large enough markets to attract competitors, even though they individually and collectively account for substantial spending.

Percentage of Reference Biologics Post Exclusivity in 2020



Put another way, the recent product launches-- including biosimilar versions of Roche's cancer drugs Herceptin, Avastin and Rituxan, are not harbingers of future widespread biosimilar launches challenging most biologics. Certain characteristics of these drugs — as well the biosimilar companies themselves — are unlikely to be representative of the overall market. Of the biosimilars approved in the last five years, the originator molecules generated an average of over \$5 bn per year at their peak. There are still no approved biosimilars for biologic products that had peak annual U.S. annual sales below \$1.3 bn. (and only one below \$2 bn., Neupogen). Notably, the 24 products that have biosimilars approved or in development have [2019 invoice sales](#) of \$2.8 bn on average, compared with just \$444 mn. for the products that don't. It is difficult for

companies to generate sufficient revenues and operating profits when the total market is smaller, so most innovator biologics just do not represent a large enough market opportunity to attract the large biopharma companies, and the manufacturing and regulatory complexity of entering with biosimilars is likely to deter smaller entrants.

Do Price Decline Provide Savings?

Biosimilars must subject innovator products to intense pricing pressure, but they don't

For biosimilar policy to produce hoped-for savings, discounts should be deep and rapid, but they are not. For the five drugs facing new biosimilar competition in the last two years, we show the pricing dynamics in Table 1. For comparative purposes, we have standardized all prices to a \$1 “filing price”, which reflects the price of the innovator biologic at the time first biosimilar competitor filed with the FDA, and where all prices are in 2020 dollars. Focusing on prices relative to the filing price makes it apparent that the first thing that happens to biologic drug prices is that they rise after the filing date. This means the first wave of ‘discounts’ offered by biosimilar entrants may seem like a good deal even if they do not come down to the level of the filing price. Three of five biosimilars did in fact enter at a discount, and at only pennies less than the filing prices (biosimilars for Avastin at \$0.91, Herceptin at \$0.92, and Epogen at \$0.95). The other two came to market higher than the respective filing prices at \$1.01 (Rituxan) and \$1.11 (Neulasta).

Also shown in Table 1, prices do continue to fall somewhat after entry, but as of 2020 blended prices hovered around \$0.90 in general. It is important to pick the appropriate comparator when assessing whether the net prices are evidence the policy goal is being achieved. Specifically, in a strongly price competitive market, residual excess profits should be driven to zero, delivering substantial savings to patients and payers. One way to gauge whether net prices are in the ballpark of what a truly competitive market might achieve is to ask if they are even below the prices the innovator manufacturer accepted prior to competitive entry – prices that by definition should be profitable to the firm. Table 1 includes a number of comparator prices for the innovator company that were accepted prior to biosimilar entry, showing that most are still well below current net prices. We also [calculated an estimate](#) of what prices would be if firms priced based on the production costs plus a 10% to 20% profit margin, that is using P-quid pricing. With conservative assumptions we estimated that the approach would produce prices in the range of \$0.25 to \$0.35, considerably below even current biosimilar prices, let alone the blended brand/biosimilar prices.

Table 1: Prices and Discounts of **Innovator** and **Biosimilar** products at key points in Innovator life cycle, normalized to \$1 at time of initial biosimilar filing. All prices were adjusted to 2020 dollars based on the Consumer Price Index.

	Avastin	Herceptin	Rituxan	Neulasta	Epogen	Enbrel	Humira
Innovator Price at Biosimilar Filing standardized to \$1 (the "Filing price")	\$1.00	\$1.00	\$1.00	\$1.00	\$1.00	\$1.00	\$1.00
Innovator Price at Biosimilar Launch	\$1.06	\$1.09	\$1.11	\$1.18	\$0.99	--	--
Biosimilar Price at Launch of First Biosimilar	\$0.91	\$0.92	\$1.01	\$1.11	\$0.95	--	--
Current Innovator Price	\$0.98	\$1.00	\$1.07	\$0.87	\$0.72	\$1.44	\$1.47
Current Biosimilar Price*	\$0.78	\$0.81	\$0.81	\$0.83	\$0.68	--	--
Average blended price**	\$0.88	\$0.90	\$0.98	\$0.85	\$0.70	\$1.44	\$1.47
Innovator Price, 2007	\$0.92	\$0.71	\$0.70	\$0.65	\$0.91	\$0.42	\$0.42
Innovator VA Price, 2007	\$0.66	\$0.50	\$0.48	\$0.55	\$0.89	\$0.23	\$0.23
Innovator UK Price, 2007	\$0.74	\$0.68	\$0.50	\$0.43	--	\$0.46	\$0.47

Sources: CMS [Average Sales Price](#)-based Medicare payment for Avastin, Herceptin, Rituxan, Neulasta, and Epogen; Wholesale Acquisition Cost for Enbrel and Humira. [Veterans Administration](#) and [British National Formulary](#). Rationale for selection of price source explained [here](#). Market share estimates from Aaron (Ronny) Gal, Ph.D., "Biosimilars (Dec. Update)," Sanford Bernstein, December 15, 2020.

Note: Epogen prices were unavailable through the British National Formulary.

* Calculated as the average price of biosimilar products weighted by their share of the biosimilar market as of 3Q2020.

** Calculated as the average price of the innovator and biosimilar products weighted by market share as of 3Q2020.

What Do Biosimilar Profit Margins Look Like?

Operating margins today are attractive to Big Pharma, but that may not be good news

Another way to size up whether the biosimilar market is shaping up as hoped is to examine the operating margins of pure-play biosimilar companies and ask whether they resemble the operating margins of companies that are under intense pricing pressure, or alternatively have considerable pricing power and protection. The operating margin reflects the

percentage of the company's revenue it retains after paying all operating expenses, and as a relevant point of reference, the median operating margins for global branded pharmaceutical and biotech companies are around 32%.

Celltrion is a large biologic manufacturer that partners with Teva and Pfizer to commercialize biosimilar products globally. The financial data (Table 2) from the most recent quarterly earnings highlight a very generous incremental operating margin even relatively early into the launch of a new biosimilar product in the US. Specifically, Celltrion launched its biosimilar versions of Rituxan and Herceptin in the U.S. (in partnership with Teva) in November 2019 and March 2020, respectively. The change in Celltrion's results between the 3rd quarters of 2019 and 2020 suggests incremental operating margin and gross margins of 59% and 69% driven largely by US biosimilar sales of Truxima and Herzuma in the U.S. If anything, rising sales in the U.S. will lead these margins to rise over time, with some analysts estimating that the operating margins for biosimilars are in the [80-90% range](#). If these projections are accurate, this underscores that the US biosimilar market is shaping up to be a very attractive and profitable business for the largest biologic products. That's nice for the players, but essentially the opposite of the highly competitive market policymakers hoped would emerge and deliver savings by driving profits down to market levels.

Table 2: Revenues and Profitability for Celltrion Healthcare (in KRW bn.)

	1Q 2019	2Q 2019	3Q 2019	4Q 2019	1Q 2020	2Q 2020	3Q 2020	Change 3Q19-3Q20
Revenues	₩220.50	₩284.80	₩282.00	₩313.60	₩356.90	₩420.30	₩463.40	₩181.40
Cost of Sales	187	248	233	224	262	292	289	56
Gross Profit	34	36	49	90	95	128	174	125
SG&A	25	27	28	47	39	41	46	19
Operating Inc	9	9	21	43	56	87	128	106
Operating Margin	4%	3%	8%	14%	16%	21%	28%	59%
Net Profit	6	9	10	41	76	46	86	76
Net Margin	3%	3%	4%	13%	21%	11%	19%	42%
Gross Margin	15%	13%	17%	29%	26%	31%	38%	69%

Policymakers might also note that the companies emerging as dominant in the US biosimilar space are primarily large established drug companies. Amgen, Biogen, Merck, Novartis, and Pfizer have launched products, or have announced

plans to do so. While it might be that all of these firms have decided to diversify into a highly price competitive sector of the market, a more likely explanation is that they have all drawn a similar conclusion regarding how the biosimilar market will evolve and it may not be the way policymakers have hoped. If we had to guess, they anticipate that adding biosimilars to their portfolio will be accretive both to their revenues and their operating profits, as both numbers have important impact on the company's share price. Put another way, pharmaceutical companies would probably not be moving into the biosimilar market in droves if they anticipated they would face cutthroat pricing and the margin pressure that would create.

Branded pharmaceutical companies have not been shy about explaining to their investors how they view the biosimilar market in the US, and it comports with our view of the market. They expect to be able to carve out their own profitable niches, taking advantage of the fact that while the costs and risks of developing biosimilars are too high for most generic and smaller drug makers, large pharma has the resources and know-how to enter. Amgen's former CFO David Meline [explained](#) that Amgen invests about \$200 mn on average to bring a biosimilar to market, in contrast with "a couple of billion to get to market with an innovative product, and ...a high risk of failure." He noted that "a capable manufacturer should have a 100% chance to get to the market with a biosimilar." While Amgen's biosimilars business is still a relatively small segment, it provides a profitable and lower-risk hedge as some of the company's large proprietary products are poised to face competition.

Conclusion

Meaningful structural obstacles to truly competitive biosimilar entry are still present in the US market, just as they were about two years ago when we argued that policymakers should not expect biosimilar competition to generate large savings. These obstacles are legion. There are technical complexities and high legal/ regulatory and manufacturing costs that impede the development of a vibrant competitive market of multiple entrants, even though that is a prerequisite to achieving the intended objectives of the biosimilar market. There are regulatory obstacles that have not been tackled, including patent thickets and litigation moats that delay biosimilar entrants with threats of treble damages and tempting "no-lose" settlement offers. These are factors in why neither AbbVie's Humira nor Amgen's Enbrel face biosimilar competition even though the products have been marketed for 18 and 22 years, respectively (well beyond the 12-year exclusivity period the FDA grants to biologic drugs). The reimbursement system in the US consistently favors drugs that cost more by relying heavily on percentage-based mark-ups for providers and other intermediaries. A raft of other substantive barriers to switching, including soft barriers such as physicians' hesitancy and operational barriers such as lack of formal interchangeability. While the FDA [finalized](#) a pathway in May 2019 (around the time of our initial proposal) for how biosimilars could be labeled as interchangeable (with the innovator biologic), [no product](#) has met the FDA's requirements and analysts generally anticipate that only a handful of relatively simple biologic products, such as insulin, will encounter interchangeable biosimilars in the market any time soon.

Policymakers are not stuck with biosimilar market competition as the only means of driving down prices and enhancing affordability of biologic drugs when they are past their exclusivity. The BPCIA intended to make the biosimilar market work like the generic market for small molecule drugs. It has failed to do so. Alternatives are available. As we suggested in 2019, a set of policies that instead required biologic manufacturers to sell their products at 'cost plus profit' after they lose FDA exclusivity would achieve the policy objectives of the BPCIA far more effectively than biosimilar entry has (or ever will). The approach as we described it, that we call [Production Plus Profit Pricing](#) (or "P-quad"), has numerous features worth [considering](#). Patents that innovators currently use to block competitors would no longer be a useful tool for forestalling price declines, as it would be the innovator itself lowering its prices. Savings would be immediate and substantial. In a recent

analysis, the consulting firm Milliman [estimated](#) that over the next five years P-quadrant could reduce net biologic spending by roughly four times the amount that biosimilars could - costs in every major payer channel decreasing by \$360 bn compared to \$95 bn from biosimilars. The biologic spending reductions derive in nearly equal measure from biologics that will not face competition at all (but should based on being past their exclusivity dates) and more effective price reductions for biologics that are or will face biosimilar competition.

Policymakers can wait yet another few years for the biosimilar market to deliver. We can then write another set of papers making the same point we did beginning in 2019. But we propose that it is time to assess the success of the BPCIA eleven years after its passage. Both evidence and market realities suggest biosimilar policy is not achieving its intended objective.