

2019 Global Biopharma R&D Productivity And Growth Ranking



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An analysis of the R&D productivity of the world's 30 largest public pharmaceutical companies reveals an overall drop in R&D productivity, but this should not hide the fact that some companies are still performing extremely well.

BY MARKUS THUNECKE AND ERIKA KUCHEN

The top companies in Catenion's annual survey have traditionally been emerging and mid-size players rather than big pharma. The same is true in 2019 as 6/10 qualify as mid-sized in the R&D ranking and 7/10 in the company ranking (that includes historical and forecast growth in sales, profit and market cap). Emerging mid-size pharma company Alexion Pharmaceuticals Inc. (a first-time entrant) and Regeneron Pharmaceuticals Inc. top the company performance ranking, but only Regeneron is in the top 10 in the R&D ranking (#8, Alexion #13). Both companies are now enjoying the fruits of their strong R&D from previous years, at the same time both are struggling to replenish their pipelines with high value assets (see Exhibit 1).

Alexion is feeling the heat as activist investor Elliott Management has a different view of the outlook than management, and the board and is pushing for a sale now. The journey from one-product success to becoming a sustainable biopharma is not an easy road, and only few companies, such as Regeneron, have succeeded without being acquired along the way. Alexion has been able to establish an industry leading complement factor franchise with Soliris (eculizumab) and Ultomiris (ravulizumab) that are expected to combine for more than \$5bn in sales by 2021. It also successfully launched Strensiq (asfotase alfa) for hypophosphatasia that is expected to achieve blockbuster sales by 2024. The issue is that there is only one higher value asset, an SOD-1 inhibitor for amyotrophic lateral sclerosis (ALS) and Wilson's disease, in its pipeline.

Another company that is struggling to

maintain its strong performance is Gilead Sciences Inc. It is still high in the ranking (R&D productivity #3), but mostly based on HIV and hepatitis C marketed products reflected in a strong long-term NPV, while the pipeline position (#16) is already pointing towards future troubles. In line with this, Gilead is also not present in the company top 10 ranking anymore (#12). After the rapid decline of its sofosbuvir hep C franchise, Gilead is highly dependent on the performance of HIV combo pill Bikarty that is responsible for a massive \$54bn in value or ca. 65% of its market cap and is forecast to peak at \$11bn in sales. Gilead's diversification strategy into oncology, culminating in the acquisition of Kite Pharma for \$11.9bn in 2017, will have to accelerate if this area is to become a serious second pillar next to its virology stronghold. CD-19 CAR-T therapy Yescarta (axicabtagene ciloleucel) is forecast to achieve blockbuster sales, but there is still a long way to go to expand patient populations and clear supply chain and reimbursement hurdles; third quarter sales in 2019 came in at only \$118m.

Oncology Is Leading The Way

In the 2019 R&D productivity ranking, oncology makes up 46% of the value across the top 30 pharma companies, dwarfing all other areas (the next in line is systemic anti-infectives with 11% and endocrine with 9%). Oncology has also seen the biggest absolute increase in value from 2018 to 2019 (followed by CNS). This value distribution is a result of the industry's increasing focus on high-unmet need specialty indications such as oncology and rare diseases.

The dominance of oncology has reached a point where it could be ques-

ABOUT THE AUTHORS:

Markus Thuncke, PhD (markus.thuncke@catenion.com), is a founding senior partner of Catenion, a biopharma focused strategy consulting firm. Erika Kuchen, PhD, is an analyst at Catenion (erika.kuchen@catenion.com).

tioned whether industry is over-spending on oncology at the expense of other areas of unmet need. On the other hand, the increasing scientific understanding of oncogenic pathways, the explosion of immuno-oncology as well as the ability to stratify patient populations make oncology fertile hunting grounds for countless biotechs and pharma companies. The analyst consensus forecast for oncology of more than \$240bn by 2024 reflects this increasing translation of scientific advances into clinical benefits.

Where Are Novartis And Roche?

Novartis AG and Roche are frequently cited as examples of outstanding R&D productivity, so why are these two companies only in the mid-field in the R&D ranking (#15 and #14)? Both had considerable success with new product launches and lifecycle extensions, but what is often overlooked is that R&D productivity is based on both value created by the pipeline and products launched in recent years, as well as the sum of R&D costs, plus adjusted costs of M&A over a 10-year period.

Both Novartis and Roche have spent considerable amounts on R&D and bolt-on acquisitions making them top spend-

Exhibit 1
R&D Productivity And Corporate Growth Ranking

R&D PRODUCTIVITY				COMPANY PERFORMANCE			
Final NPV Rank	Company	Momentum (Pipeline NPV)	Long-Term (All NPV)	Final Corp. Growth Rank	Company	Past Performance	Forecast Performance
1	AstraZeneca	12	3	1	Alexion Pharmaceuticals	1	1
1	Biogen	3	6	2	Regeneron Pharmaceuticals	4	5
3	Gilead Sciences	16	2	3	Novo Nordisk	5	6
3	Eli Lilly	1	7	4	Johnson & Johnson	11	9
3	Novo Nordisk	19	1	5	Amgen	7	14
6	Amgen	6	9	5	Bristol-Myers Squibb	9	12
7	Merck & Co	23	5	5	Allergan	2	19
7	Regeneron Pharmaceuticals	26	4	8	Merck & Co	14	8
9	GlaxoSmithKline	7	12	9	Eli Lilly	14	10
10	Astellas Pharma	5	15	9	Eisai	23	1

TOP 5

SOURCE: Catenion

ers over the 10-year period included in this analysis: in 2018 Roche spent \$9.8bn on pharma R&D (#1) and Novartis \$8.2bn (#3). To create value through such enormous R&D spending, the portfolio value *increase* has to match at least the \$8bn-\$10bn p.a. plus a large sum (more than \$1bn) that is typically spent on bolt-on acquisitions. It is tremendously difficult to implement a scalable model of superior R&D productivity.

Productivity Champions

There are four large pharma companies that have high positions in the 2019 R&D ranking, the most notable one is back-to-back winner AstraZeneca PLC, sharing the #1 spot with Biogen Inc. The only reason why AstraZeneca does not have a top spot

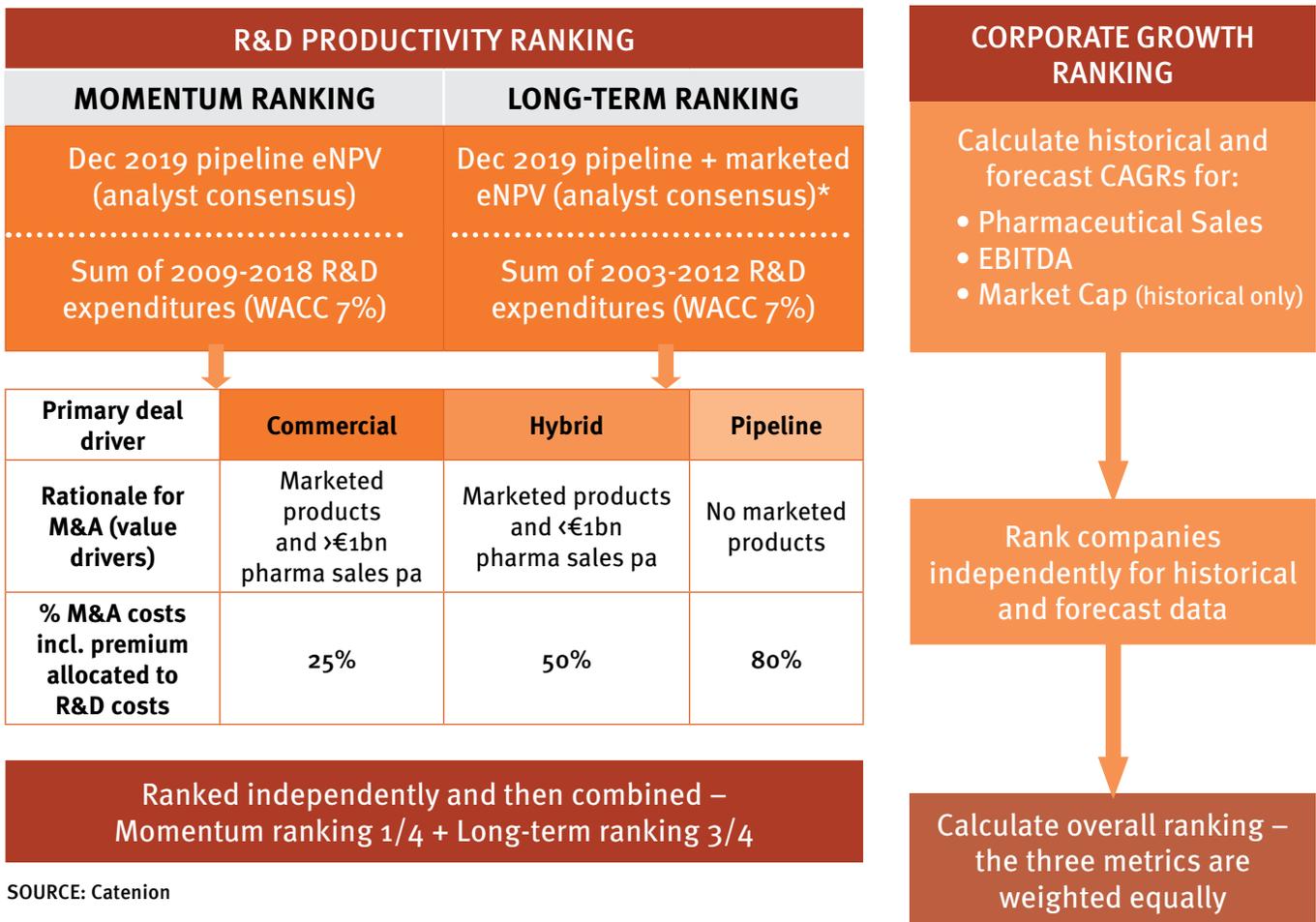
in our Corporate performance ranking is its poor past performance (#26), while the forecast performance reflects its strong R&D productivity (#4) spot.

AZ's impressive turnaround story that started with the arrival of Pascal Soriot from Roche continues: its two biggest products both in terms of value and potential are EGFR inhibitor Tagrisso with \$40.4bn in value and \$8bn in forecast peak sales, followed by PD-L1 inhibitor Imfinzi (durvalumab) with \$24bn in value and \$5bn in forecast peak sales. The AstraZeneca case exemplifies that a complete turnaround is possible even for big pharma companies that many people had already written off. The mixture of strong leadership who realize the solution is not another round of mega mergers

but a focus on R&D rejuvenation could be a template for other large organizations who find themselves in a similar position.

Biogen's top position may seem unexpected when considering the initial difficulties with its Alzheimer's antibody aducanumab that had been discontinued after an interim futility analysis in Phase III in March of 2019. Since then, the events took an unexpected turn upon re-analyzing the data and finding a positive signal in one of the two Phase III studies in October 2019. Consultations with the FDA led to the decision to file for approval. It was one of the most unusual biopharma stories of 2019, especially as this is not only about aducanumab but also about the validity of the beta-amyloid hypothesis, that was largely dismissed after the nth Phase III

Exhibit 2
Method Used To Calculate R&D Productivity



SOURCE: Catenion

failure in a row.

Beta-amyloid has now staged a comeback, and many stock analysts have re-entered aducanumab into their Biogen valuation models as the lone high value asset in the pipeline (\$2.2bn peak sales to Biogen, \$4.4bn NPV). Due to the uncertainty of the drug reaching the market and the high pipeline value concentration, Biogen’s current position as a top company is definitely at risk as recently launched spinal muscular atrophy blockbuster Spinraza (nusinersen) may not be sufficient to compensate a declining portfolio of multiple sclerosis blockbusters. Biogen’s difficulties are typical symptoms shared by many of the mid-sized outperformers of the last years that face huge challenges. Simply put, it is difficult to maintain the creative culture and performance focus that made these companies great as they go through periods of hyper-growth.

Novo Nordisk Sits Pretty In Top 5

Novo Nordisk AS is the only company that has defended a top five position in the ranking since its inception in 2014. In this year’s survey, Novo Nordisk is the only company to be in the top five in both the R&D Productivity and Company Performance rankings. Novo Nordisk is a prime example of the power of highly focused R&D in the endocrinology space as 80% of sales stem from internal R&D and 86% fall into the endocrinology area, mostly peptides and proteins. Its largest product is Ozempic (semaglutide), the leading GLP-1 agonist in an ever growing diabetes market (\$25.9bn in value and \$7.4bn in peak sales), the oral version of which has just been approved in the US (Rybelsus) and is forecast to be another mega-blockbuster (\$14.5bn in value and \$5.6bn in peak sales).

The main strategic question for Novo Nordisk is whether they can keep up that

kind of outperformance. The mid-term outlook appears very strong as loss of exclusivity of semaglutide is not before 2031, this should give Novo Nordisk enough runway to diversify into other areas such as obesity, NASH and diabetic complications. Interestingly, Novo Nordisk has unsuccessfully tried several times already to diversify into areas such as inflammation, oncology or neuroscience. Perhaps its lack of traction in these areas is unsurprising given the enormous success of its core franchises (Clayton Christensen’s innovators dilemma comes to mind). One of the key drivers of Novo Nordisk’s long-term success is its unique model and set-up as a public company that is fully controlled by a foundation. The Novo Foundation protects Novo Nordisk from being acquired while ensuring that its unique mixture of altruistic and business motives embedded in the “Novo Nordisk Way” are kept alive.

Lilly Enters Top 10

Lilly Research Laboratories's #3 spot in R&D Productivity comes as a real surprise (last year #10) as its R&D organization has kept a very low profile over the last few years. A closer look reveals that its strong performance is fueled by a successfully growing diabetes franchise, with GLP-1 agonist Trulicity (dulaglutide) leading the way; this asset has seen a massive increase in value from 2018 to 2019, representing \$23bn in value and \$6.7bn in projected peak sales. Strengthening the GLP-1 franchise is tirzepatide that was not included in most analyst models last year but is expected to become a large product with \$8.9bn in value.

Lilly's second largest product Taltz (ixekizumab), a psoriasis antibody, has also increased since last year to \$2.5bn in peak sales and \$8.2bn in value. As Lilly is new to the top five, it will be interesting to see how sustainable this much-improved performance is, in 2019 it has already translated into a top 10 spot in the Corporate Performance ranking (#9).

The most exciting move the company has done in a long time was the acquisition of Loxo Oncology for \$8bn, even though the lead product Vitrekvi (larotrectinib) was already licensed to Bayer. Lilly will get royalties and an interesting pipeline of targeted therapies in oncology such as a next generation BTK inhibitor. The acquisition is a first step towards an increasing focus on oncology, a theme seen with the other major turnaround story in this year's ranking, AstraZeneca.

What Really Matters?

In spite of industry-wide problems with R&D productivity, Catenion's annual survey has demonstrated over the years that it is possible to outperform and to create substantial value for patients and shareholders. So what are the common denominators among the top ranked companies? Catenion has identified a few elements that contribute to sustainable R&D outperformance that translate into superior growth and profitability:

- A science-driven innovation culture and model: a prime example is Regeneron whose model resembles the Genentech of the 90s with its focus on people and

culture as competitive advantages.

- Establishing a clear competitive advantage: building disease area strongholds and industry leading R&D capabilities. Examples are Novo Nordisk in endocrinology and proteins or Gilead in virology.
- Focus on high unmet need specialty indications: the market growth of oncology as well as the rich scientific and drug target landscape make it the industry's most popular area. The role of oncology in AstraZeneca's turnaround story is an illustration of this approach. Smaller bolt-on acquisitions: instead of major M&A, smaller bolt-on acquisitions complemented by licensing has been the strategy of choice for most top 10 companies, the notable exceptions being Novo Nordisk and Regeneron that have completely relied on internal R&D strength.
- Strong presence in US market: the US is responsible for a disproportionate part of the global biopharma profit pool. In addition, hotbeds such as Boston ensure the US keeps a leading position in the global biopharma innovation system in terms of talent and output.
- Effective portfolio decision-making: the much-cited truth seeking versus progression seeking behaviour is at the root of effective portfolio governance that was a main factor in the turnaround of AstraZeneca. This is one of the most underutilized and cost-effective levers that exists.

The examples of R&D productivity champions create hope for those companies that find themselves at the bottom of the ranking. The AstraZeneca case study demonstrates that R&D productivity is not just based on luck but on strong leadership. This emphasizes the importance of people, culture and model as the foundations of competitive strategy.

Methodology:

R&D Productivity Ranking

In order to evaluate the R&D productivity of the world's 30 largest public pharmaceutical companies, as judged by total pharmaceutical sales, the Catenion methodology takes an approach that focuses on value. It compared the total R&D spending from 2009-2018 including costs from M&A (see Exhibit 2) and a 7%

cost of capital with the total net present value (eNPV) today of compounds marketed in the last five years and all pipeline products.

Using this data, two distinct rankings were calculated – a "Momentum" and a "Long-Term" ranking. The Momentum ranking aims to capture the value a company is forecasted to generate by taking the current eNPV of its entire pipeline and dividing by the firm's R&D and M&A costs, both adjusted for cost of capital, as described above. By contrast, the Long-Term ranking focuses on the value a company has already generated in the recent past, specifically the eNPV of products marketed in the last five years are added to the pipeline eNPV whilst those marketed six to eight years ago are also added but with the contribution tailing off by 33% per year. This is then divided by the total costs as per the Momentum rank.

The overall R&D Productivity rank was then generated by weighting the momentum rank 1/4 vs. 3/4 for the long-term rank.

To fairly allocate M&A costs to the R&D costs, each deal was defined by its primary driver. If the acquired firm had pharma sales >€1 bn then was said to be commercial and thus 25% of the deal total deal value was added to the R&D costs for that year. By contrast a deal involving a firm with no marketed products is, by definition, a pipeline driven deal, thus 80% of the deal costs were taken. In addition, if the total cumulative sales of the target company up until the deal date were <20% of the deal value then these were also considered to be a pipeline driven deal (e.g. AbbVie Inc.'s acquisition of Pharmacyclics). Finally, if a firm had pharma sales <€1bn then it is considered a hybrid of the two deals and thus 50% of the M&A cost were used.

Corporate Growth Ranking

To evaluate the corporate performance of each firm, the historical and forecasted CAGR for pharmaceutical sales, EBITDA and market cap (historical only) was calculated. Each company was ranked independently on each of the five metrics before they were combined with equal weighting to generate the overall corporate growth ranking. ❁

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