

Value-Based Pharma R&D Productivity: Is There A Sweet Spot?

What do Gilead, Biogen, and Celgene have in common? Qualities to be the top three drugmakers ranked by both R&D productivity and growth, according to a novel method for measuring such criteria that management consulting firm Catenion says offers insights for achieving such success.

BY MARKUS THUNECKE, GRAHAM SCHOLEFIELD, AND CHRISTOPHER MEYER

- The best performers have a strong focus on certain specialty disease areas and a high percentage of revenues from the US market.
- The highest ranked companies all have strong internal R&D capabilities and tend to in-license or acquire assets at an earlier stage than the rest.
- An R&D budget of around €1 billion (\$1.4 billion) to € 2 billion (\$2.7 billion) defines the sweet spot where companies both have critical mass and are at their most productive.
- Bureaucracy associated with size and the loss of creativity is a clear barrier to R&D productivity and market success and further questions the logic behind the M&A-driven strategy of most Big Pharmas.
- But the most important factors are a strong culture and leadership team that attract and keep the high-caliber people who are ultimately more important for success than just assets and technologies.

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Commercial and R&D successes achieved by **Biogen Idec Inc.**, **Gilead Sciences Inc.**, and **Celgene Corp.** show that strong performance is still possible in an industry struggling with patent cliffs and poor R&D productivity. While that elite trio is relatively young – with a strong biotech heritage – there are also highly successful large pharma companies such as **Bristol-Myers Squibb Co.** that have completely turned around their R&D and corporate performance in recent years and are performing well.

We have introduced a systematic approach for identifying the R&D outperformers among the top 30 pharma companies, and we have explored a number of key questions, such as:

- What are the common elements among the best performing companies?
- Does strong R&D performance always translate into corporate growth?
- Is there an optimal size for an R&D organization in terms of budget, a so called sweet spot?
- Is a mega-merger really a solution to fix long-term performance of a pharmaceutical company?

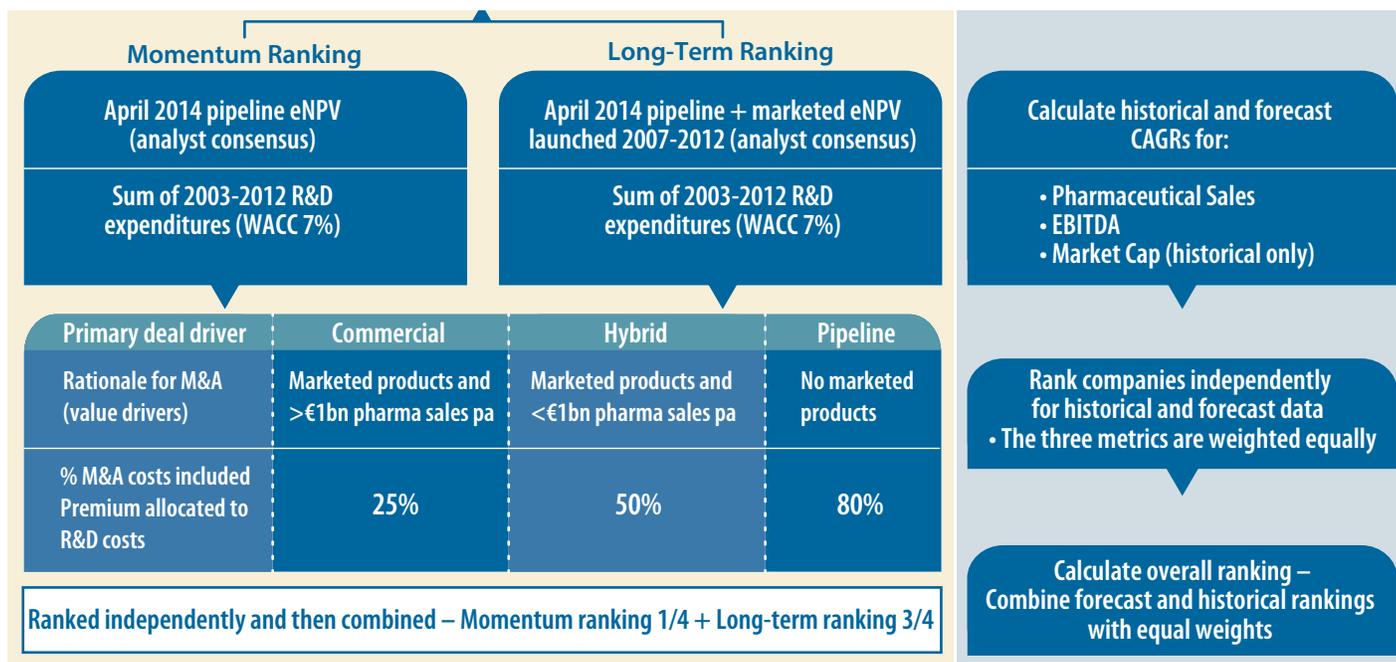
This approach differs from two studies conducted in recent years that reviewed R&D productivity by looking at total output in terms of approved drugs and relating that to total R&D spending over a defined period.

Bernard Munos, in his article “Lessons from 60 years of pharmaceutical innovation” published in *Nature Reviews Drug Discovery* in 2009, looked at new molecular entity (NME) output and spending from 1950 to 2008 and found that it is virtually impossible to increase NME output to more than one per year per company, irrespective of total spending.

In early 2013, Matthew Herper of *forbes.com* also reviewed NME output from a 10-year period versus cumulative spending. His key conclusion was that cost per new drug for large companies – those that had launched more than three NMEs in the preceding 10 years – was between \$4 billion and \$5 billion. This is an unsustainably high cost when compared with the previously reported price tag of some \$1 billion per NME.

Exhibit 1

Overview Of The Ranking Methodology



SOURCE: Catenion analysis

Neither of those studies considered the actual value created by the R&D investment, despite this being a much more important measure for the overall performance of a company than just the number of approvals.

Clearly, it makes a big difference whether one gets the equivalent of an *Avastin* [bevacizumab] approved, which had sales of \$7 billion in 2013, or a *Zevalin* [ibrutinomab tiuxetan], which generated revenue of \$35 million in the same year.

Nor did the earlier two studies analyze the size, or quality, of current pipelines.

Catenion’s methodology calculates R&D productivity and its influencing factors seen from a value perspective (See Exhibit 1). It used the top 30 public companies measured by total pharmaceutical sales and compared their cumulative R&D spending from 2003 to 2012, including costs for M&A and a 7% cost of capital, with the risk-adjusted net present values (eNPVs) of marketed products launched in the last five years and pipeline products.

From this, two rankings were compiled – a “Long-Term Performance” rank, which includes eNPVs for products launched in the last five years as well as the entire pipeline, and a “Current Momentum” rank, which only uses pipeline eNPVs.

These two were then weighted and combined to give the overall “R&D Productivity”

ranking. (Complete methodology available in the online version of this article)

Also created was a corporate growth performance ranking built from two elements: corporate “Past Performance” and “Forecast” growth metrics.

The Past Performance measurement consists of the 10-year average CAGR (compound annual growth rate) of sales, EBITDA (earnings before interest, taxation, depreciation, and amortization), and market capitalization. The Forecast growth metric is the five-year average CAGR projection of sales and EBITDA.

These two formulas were then equally combined to yield the “Corporate Growth Performance” ranking.

GILEAD, BIOGEN, AND CELGENE TOP TABLES

The R&D Productivity and Corporate Growth Performance rankings were compiled during April 2014; two tables display the top 10 companies in both categories. (See Exhibit 2.) From the table it can be seen that the top companies Gilead, Biogen, and Celgene correlate across the two rankings, indicating exemplary R&D productivity translates into superb corporate growth.

But this relationship breaks down toward the bottom of the ranking (not shown), im-

plying that other factors are also important such as launching old products in emerging markets, raising prices in established markets, having a high share of biologics that have not yet been affected by biosimilars, as well as cost cutting – steps that can offset poor R&D for a time, but in the long run patent cliffs will threaten to bring down even the most resilient performers in the absence of strong innovation. (See Exhibit 3.)

One example is Germany’s **Merck KGAA**. A laggard (bottom five) in the R&D ranking, it nonetheless holds a mid-field Corporate Growth position. Its portfolio consists largely of specialty biologics that have so far benefitted from the later than expected impact of biosimilars.

The German conglomerate also has a number of older pharma products that have a second life in emerging markets, and it has recently gone through a major corporate re-structuring and cost cutting. For a while, all these levers can compensate for a poor R&D engine, but in the long run Merck KGAA’s future performance will critically depend on innovative new drugs as its main lifeblood. For that reason, the company completely overhauled its R&D model and strategy in 2012.

The opposite can also happen, where a strong R&D engine is undermined by patent cliffs and sub-par commercial performance.

Exhibit 2

R&D Productivity And Corporate Growth Ranking, Top 10 Companies

R&D PRODUCTIVITY				CORPORATE GROWTH			
FINAL NPV R&D RANK	COMPANY	LONG-TERM (ALL eNPV)	MOMENTUM (PIPELINE eNPV)	FINAL CORP. GR. RANK	COMPANY	PAST PERFORMANCE	FORECAST PERFORMANCE
1	Gilead Sciences	2	2	1	Gilead Sciences	2	1
2	Biogen Idec	3	3	2	Celgene	1	2
3	Celgene	5	5	3	Biogen Idec	5	3
4	Bristol-Myers	7	1	4	CSL	4	6
5	Novo Nordisk	6	8	5	Shire	7	4
6	Shire	4	16	6	Allergan	10	8
7	CSL	1	30*	7	Novo Nordisk	6	13
8	Johnson & Johnson	8	24	8	Bayer	11	7
9	Chugai Pharmaceutical	15	6	9	Roche	14	10
10	Novartis	11	19	10	UCB	19	5

Big pharma (>€15bn sales 2012) **bolded**; final R&D productivity rank is generated by weighing all NPV 3/4 and Pipeline NPV metric 1/4; *No pipeline NPVs available
SOURCE: Catenion analysis

BMS is a good example, as its R&D performance places it in the top five but it ends up only in the mid-field in terms of corporate growth. One can expect, though, that in the long run the strong R&D engine of BMS will prevail.

TOP PERFORMER QUALITIES

The common elements in this elite group of top R&D performers identified in this analysis can be summarized as follows:

- **Not Too Large.** The R&D budgets are between around €1 billion (\$1.4 billion) and €2 billion (\$2.7 billion), and the R&D organization has between 500 and 700 people per site. Such sized companies can reap the benefits of critical mass covering essential technologies and skills with broad enough scope and depth within focus areas, while still having a strong culture and room for individual initiative and creativity.
- **Higher Degree Of Focus.** Gilead was initially focused exclusively on HIV but diversified into HCV and oncology, mostly through deals and acquisitions. Celgene was initially focused on hematological malignancies and has now expanded into

solid tumors and inflammation. Biogen is highly focused on neurology and inflammation, having decided to exit oncology a few years ago, a previously unheard of move, as most companies wanted to enter oncology as the hot new growth area. As a sidenote, the recent off-loading of GlaxoSmithKline's oncology portfolio to Novartis AG can also be interpreted as a way of increasing both companies' portfolio focus.

- **Higher Value Concentration In Their R&D Portfolio** than average or poor performers. In addition, the top performers have all established a multi-asset portfolio of marketed products and are no longer fully exposed to the dangers of market withdrawal or Phase III failures. US-Focused. Four out of five outperformers are US-based drugmakers that derive a major part of revenues from the US market. Even the only non-US company, Danish Novo Nordisk AS, generates half its sales there.
- **Focused Business Development And Licensing Mix.** The top five companies in the R&D ranking all have strong internal R&D capabilities but are also very active

dealmakers. Top performers bring in more projects earlier (pre-Phase III) than less successful peers. In summary, BD&L has become a standard source of growth that is at its most effective when supported by strong internal capabilities.

- **Unique R&D Models.** All top larger pharma companies in the ranking have implemented unique R&D models, relying on strong focus, disciplined capital allocation, and selective acquisitions.

ROADMAP TO SUCCESS?

The authors believe their findings offer a roadmap to success when viewed in the journey of outperformers so far. Signposts include aiming for a sweet spot in terms of size – both people per site and overall R&D budget, having a focused R&D approach, and building deep internal capabilities complemented regularly by in-licensing and selective smaller-scale acquisitions as strategic levers. And most importantly, to succeed companies must have strong leadership and a science-driven culture with a real sense of purpose. (*See "What Can The*

Exhibit 3

Correlation Between R&D And Corporate Growth Performance

		CORPORATE GROWTH RANKING			
		OUTPERFORMERS	MID-FIELD		LAGGARDS
R&D PRODUCTIVITY RANKING	OUTPERFORMERS	Biogen Idec Celgene Gilead Sciences	Bristol-Myers Squibb Novo Nordisk		
	MID-FIELD	CSL* Shire	Abbott Amgen Astellas Bayer Chugai Daiichi Sankyo	Johnson & Johnson Merck & Co. Mitsubishi Tanabe Novartis Otsuka Roche UCB	AstraZeneca Eli Lilly GlaxoSmithKline Pfizer Takeda
	LAGGARDS	Allergan	Baxter Merck KGAA Sanofi		Eisai

*Pipeline NPVs for CSL were unavailable. Three categories (outperformers etc.) are based on performance rankings, top 5 = outperformers, bottom 5 = laggards, companies in each bucket are ranked alphabetically not by performance.

SOURCE: Catenion analysis

Biopharmaceutical Industry Learn From Apple Inc.?" — IN VIVO, January 2014.)

In the end, two important questions remain for the current crop of mid-size biopharma outperformers that are currently firmly embedded in the sweet spot: can they keep it up as they go through a period of hyper-growth? Can their model be scaled to the next level of size and productivity or are they doomed to lose focus and turn into the next **Merck & Co. Inc.**, which went from America's most admired company to an underperformer within a decade? These questions will be discussed in the second part of this article, "R&D Productivity: Is There A Scalable Model?" to be published in *IN VIVO* this fall.

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LUCK OR STRATEGY?

Serendipity or luck has always played a role in the risky sector of biopharmaceutical R&D. The authors strongly believe luck can accelerate what is already a strong model and culture.

The elite group of R&D outperformers each made it through difficult periods and ultimately succeeded in launching not only one major drug – which could have been luck – but several drugs, sometimes through smart acquisitions, becoming even more shielded from catastrophic events, such as market withdrawals.

Celgene, for example, has demonstrated a mixture of focused experimentation, perseverance, and luck ever since its foundation as a spin-off from chemistry giant Celanese in 1986 to commercialize its capabilities in chiral chemistry and manufacturing. Several failed revenue models followed including biotreatment (discontinued in 1994) and selling chiral intermediates to pharmaceutical companies (that business was sold in 1998). The company then stumbled upon thalidomide and initially got an approval for leprosy, before licensing the oncology rights from **EntreMed Inc.** in 1998. Between 1996 and 2005 the company ran over 150 clinical trials with thalidomide, mostly leveraging third parties, in numerous indications to finally settle on multiple myeloma, getting it approved in 2004. Celgene was then able to use its expertise in chemistry to find follow-on molecule *Revlimid* (lenalidomide). It seems to be a common theme that today's outperformers initially cast a broad net, but once promising signals were found they then executed with admirable focus and perseverance.

It was a similar story for Biogen in the field of interferons. More recently, the company also survived a very difficult period in its history that ended with the hiring of George Scangos as CEO and Doug Williams as head of R&D to uncover the science-driven culture and model that made it great in the first place.