

# Value-Based Pharma R&D Productivity: Is There A Scalable Model?

The superior R&D and growth performance of companies like Celgene, Gilead, or Biogen can be attributed to a number of factors such as the size of the R&D budget, a high degree of portfolio focus, a good mixture of internal and external innovation sourcing, but most importantly a strong culture, leadership, and the ability to attract the right people.

BY MARKUS THUNECKE

- The billion-dollar question for the current crop of mid-size biopharma outperformers is whether their model can be scaled to the next level.
- On a conceptual level, larger R&D organizations should be able to benefit from greater knowledge diversity as a key driver of cross-fertilization or serendipity, which lie at the core of most of pharma's breakthroughs. In reality, however, these advantages are neutralized by organizational silos, politics and the loss of strong culture and leadership.
- Among the critical dimensions for growing high-performance R&D organizations: R&D budget growth trajectory, leadership capacity, and degree of internal and external collaboration.

Caution's systematic review of R&D productivity and corporate growth metrics shows that size correlates negatively with performance from a certain point onward. (See "Value-Based Pharma R&D Productivity: Is There A Sweet Spot?" — IN VIVO, June 2014, in which we reviewed 10-year cumulative R&D spending adjusted for costs of M&A versus value created in the pipeline and products launched over the last five years, plus growth in topline, EBITDA, and market cap for the top 30 public pharma companies.)

In our survey, all top performers are mid-size companies; mostly with a biotech heritage, such as **Gilead Sciences Inc.**, **Biogen Idec Inc.**, or **Celgene Corp.** The 'Sweet Spot' lies between €1 to 2 billion total R&D budget. Companies that are much smaller often don't have the critical mass and they are still fully exposed to portfolio risks (i.e., most smaller biotech companies fail to deliver a meaningful return to shareholders), whereas companies much larger lose the creative spark that made them successful in the first place.

## CAN THE CURRENT OUTPERFORMER MODEL BE SCALED?

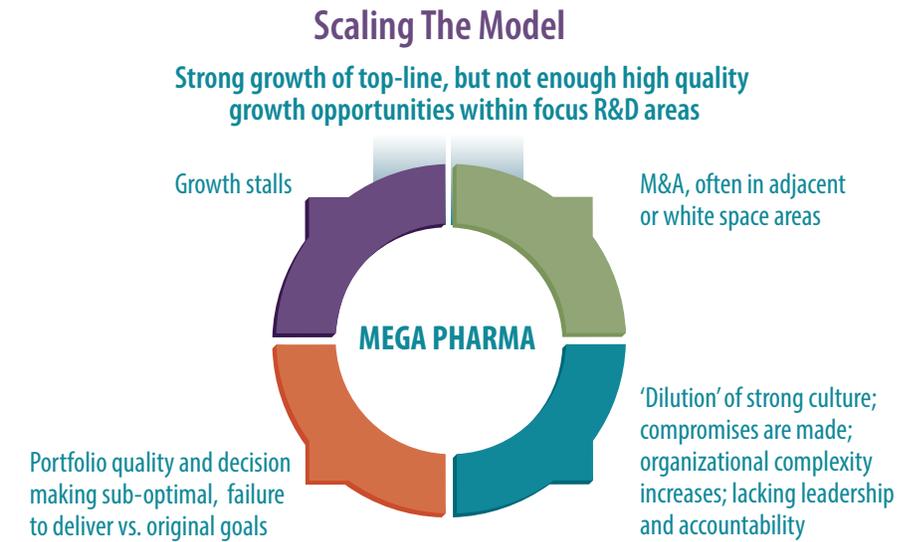
The implications of the above are significant for the current crop of R&D outperformers: Can Celgene, Biogen et al. grow without losing the creative spark that made them so successful? The tight link that seems to exist between topline growth and the R&D budget can also be a significant hurdle, as doubling in size over a five year period implies a doubling of the R&D budget as well, although it can be questioned whether there are really enough high quality opportunities to invest in? Typically companies in that situation start diversifying and sometimes losing their way through ill-advised acquisitions, overstretching of core capabilities etc. (See *Exhibit 1*.) An example is the increasing popularity of oncology as a hot growth area. As a result, many large and mid-size pharmas have active oncology R&D efforts and many of those

not yet present are contemplating an entry. The fact that it often takes decades to build the deep capabilities required to succeed in that highly complex area can be overlooked when companies seek new investment areas and quick successes (a recent Catenion study shows that the number of drug treatable patients per expected launch based on pipeline size is ~10,000 in oncology compared to e.g. >100,000 patients in the immunology field.) Interestingly, Biogen decided to exit oncology recently whereas Gilead has entered the field as it is seeking growth opportunities outside of the maturing HIV and increasingly competitive HCV markets. The recent portfolio swap between **GlaxoSmithKline PLC** and **Novartis AG** in oncology took many observers by surprise as it signaled that even a massive R&D organization like GSK's did not think that it could be successful in oncology.

**WHAT ARE THE OPTIONS FOR BIG PHARMA?**

Within large pharma the fundamental problem is similar but in a different context; here the question is often one of corporate survival at the current scale. Although there are numerous studies that demonstrate how mega-M&A destroys value, some executive teams still regard it as an appropriate strategic response in times of lacking growth prospects. **Pfizer Inc.**'s pursuit of **AstraZeneca PLC** is a recent example, but has to be viewed with great skepticism against the backdrop of

Exhibit 1  
**The Vicious Circle Of Growing R&D**



SOURCE: Catenion

the results from our R&D productivity survey. When two poor performers combine (both are in the bottom tercile in our rankings), why should that address any of the fundamental questions that have not been answered in either company? While a few years of time can be 'bought' through cost cutting and realization of synergies, the price is usually too high as M&A will only further disrupt the most critical and creative parts of an organiza-

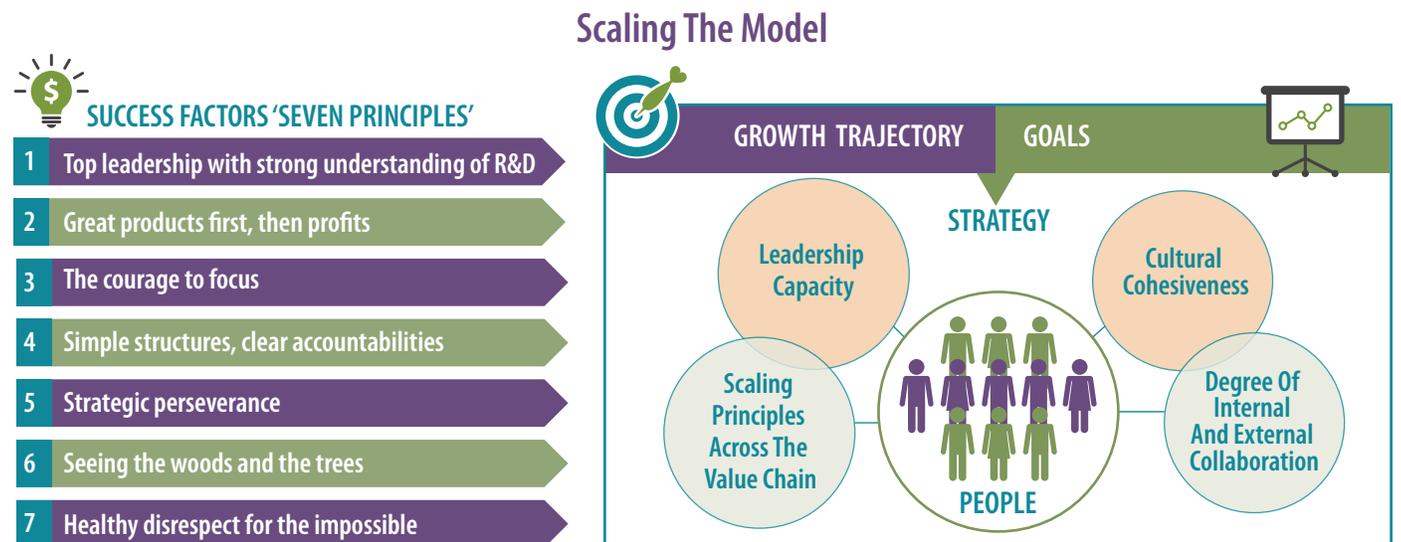
tion, and the original problems are inevitably bound to return, only on a much larger scale.

**POSSIBLE GROWTH MODELS**

There are a number of academic studies that investigate the fundamental problem of innovation in large organizations. Clayton Christensen, in his 1997 book 'The Innovator's Dilemma' used the computer industry to show how the incumbents, stifled by their complacent culture and arrogance, are often

Exhibit 2

**A Framework For Scaling High Performance R&D**



- SUCCESS FACTORS 'SEVEN PRINCIPLES'**
- 1 Top leadership with strong understanding of R&D
  - 2 Great products first, then profits
  - 3 The courage to focus
  - 4 Simple structures, clear accountabilities
  - 5 Strategic perseverance
  - 6 Seeing the woods and the trees
  - 7 Healthy disrespect for the impossible

SOURCE: Catenion

## SUCCESSFUL R&D PERFORMERS

**Bristol-Myers Squibb Co.** is by far the best performing large pharma company and it has managed a successful turnaround since 2006 when the company was suffering from poor R&D performance and lacking growth prospects. The then new R&D head Elliott Sigal, MD, PhD, has put in place a model that combines a strong emphasis on innovation, partnering across the value chain and a culture of continuous improvements. Elliott Sigal believed that merely mimicking a biotech company was not going to work, thus the BMS slogan of combining the 'best of biotech and the best of pharma'. Its biggest break, however, came when BMS acquired Medarex Inc. as part of its 'chain of pearls strategy'. This brought them an oncology immunotherapy platform with *Ipilimumab* and *Nivolumab*; both compounds are now the biggest value drivers in the portfolio.

**Johnson & Johnson** has a decentralized approach to business in general, and compared to other companies grants more autonomy to its numerous operating companies. It has become a master of avoiding Christensen's 'innovator's dilemma'. J&J's values, embedded in its 'Credo' are the cultural glue that holds all the different pieces of its empire together. The R&D model is based on end-to-end TAs with distinct leadership teams, reporting into the Head of R&D, Bill Hait, MD, PhD. Strong leadership is ensured at the highest level of the company through Paul Stoffels, MD, who acts as J&J's CSO and had the benefit of learning under the legendary Paul Janssen, PhD. The company also stresses external innovation through a number of external hubs.

The third model that can serve as an example on how to scale innovation is **Novartis AG**. It also has its roots in the strong leadership commitment that started with former CEO Daniel Vasella, MD, who hired Marc Fishman, MD, an academic scientist without prior drug development credentials, to implement a novel science-driven Research and Early Development organization in Boston, the Novartis Institute for Biomedical Research (NIBR). Fishman was granted an unusual degree of autonomy and his mandate was to 'reinvent the grammar of drug discovery'. His new model combined a strong belief in the power of science vs. commercial considerations and it emphasized the then emerging field of translational medicine to help make better choices in early development.

Although currently not among the top 10 in R&D performance, **Roche** can also provide some valuable lessons. The company implemented a 'hub-and-spoke' R&D model in the 90's which ultimately allowed **Genentech Inc.** and **Chugai Pharmaceutical Co. Ltd.** to retain independence. Former R&D Head Jonathan Knowles, PhD, strongly believed in the value of smaller, autonomous units and the echo of this can still be found in the decision to not integrate Genentech Research and Early Development into the rest of the Roche R&D organization.

out-innovated by small upstarts that come up with products that are initially not taken seriously or even underperform. His conclusion was that when an incumbent faces a potentially disruptive technology an attractive option is to create a spin-off in order to prevent unhealthy influence from the mother company. Within our context, Christensen's observations are highly relevant. Just consider the case of monoclonal antibodies, where the established small molecule companies missed the boat in the 1980s and '90s and it was biotech compa-

nies like **Genentech Inc.** that realized most of the early value of the technology. In an interesting spin of fate the pharma part of German chemicals giant **BASF AG** (Knoll AG) had signed a deal with Cambridge Antibody Technology PLC in 1993, leveraging its focus and expertise in the antibody field. Out of that deal came *Humira*, one of the most successful and valuable drugs ever (€8 billion sales in 2013), but BASF had decided to sell Knoll including Humira to **Abbott Laboratories Inc.** for €5 billion in 2000. Just imagine what value BASF could have created, had it decided to

spin off the novel technology into a new fully owned daughter company and let it run. It is easy to be right with the benefit of hindsight, but this anecdote exemplifies a more general weakness of incumbents to realize the potential of an emerging technology against the backdrop of a successful base business.

In spite of all the talk about the R&D productivity crisis, there are a number of firms that have bucked the trend and have successfully grown far beyond the most productive 'sweet spot' of €1-2 billion R&D budget. Their strategy and models can provide some interesting lessons: **Bristol-Myers Squibb Co.**, **Novartis** and **Johnson & Johnson**. (See sidebar, *Successful R&D Performers*.)

The R&D performance of these larger companies will most likely not enable hyper-growth à la Celgene or Gilead but it still demonstrates that it is possible to create a good return on R&D investments even at a much larger scale than that of the current mid-size R&D outperformers. These companies all went to great lengths to reinvigorate R&D, often through substantial restructuring, and they were patient enough not to expect results within one or two years. They also found organizational solutions to avoid an 'innovator's dilemma'. But the most important success factors are strong and consistent leadership and the realization that a good model and science-driven culture are the starting points for turning around R&D performance.

### A FRAMEWORK FOR SCALING HIGH PERFORMANCE R&D

So what are the factors that drive high-performance R&D in larger organizations? In a previous article (see "*What Can The Biopharmaceutical Industry Learn From Apple Inc.?*" — IN VIVO, January 2014), we emphasized the importance of a tech-savvy leadership, and a number of cultural and organizational factors ('seven principles'). We've also discussed the intrinsic advantage of being in the 'sweet spot' (€1 billion+ R&D budget) that has enabled strong growth and created a new breed of biopharma outperformers. The much harder task is to stay among the outperformers. BMS, Novartis and J&J have successfully scaled performance to a much larger level, often sharing some common elements and principles.

In our view, those executive teams that want to build a successful and scalable high

performance R&D model should ask themselves a number of fundamental questions: (See Exhibit 2.)

**1. What is the long-term growth trajectory and what will be the impact on the R&D budget, the strategy, and the ability to grow the portfolio?** Suppose for example that a company is forecast to double in size in the mid-term: if one assumes that the R&D budget grows at the same rate, are there really enough high-quality investment opportunities within the current strategy? Often the conclusion will be that there is a significant gap, and the knee-jerk reaction may be to seek external growth to 'justify' a high R&D budget. In our scaling framework this automatism no longer exists and the R&D budget should depend on the opportunities and not just be driven up as a percentage of topline growth. Obviously, this requires a flexible operating model that can 'breathe' as required.

**2. What is the leadership capacity of the senior executive team?** Where are the constraints? Is the leadership capable to effectively govern a much larger and broader portfolio? If the leadership team is out of its depth (which takes a great deal of honesty and self-reflection to admit), it speaks for spinning off and delegating accountability for that portfolio to a different unit. The case of the lowly ranked Big Pharmas in our R&D

productivity assessment should be a warning signal, as it speaks to the impossibility of effectively governing a portfolio on that scale.

**3. Can enough talented people that fit the required profile and culture be recruited during the hyper-growth period?** Although this may sound simple, maintaining high standards is not easy when hundreds of new people have to be recruited and on-boarded in a comparably small timeframe.

**4. Does the new growing company have sufficient 'cultural cohesiveness'?** The author has experienced a typical hyper-growth company that recruited people who came from various Big Pharma backgrounds. This created a true melting pot, however, as no strong corporate culture existed it made it incredibly hard to act and feel as 'one company', as most people fell back on their legacy organizations ('this is how we have done things at Pfizer/Novartis/Amgen...'). Having a strong science-driven culture with a real sense of purpose and a leadership that truly embodies that is a clear differentiator and possibly the most important success criterion for building a high-performance R&D organization.

**5. Do we have a deep understanding of 'scaling principles' across the value chain?** Where does it really matter to be big, and where is it a barrier to creativity and innovation? In our own experience some functions and disciplines can benefit greatly from

economies of scale, while others are often impacted negatively. The core knowledge creation units of a R&D organization should not be too large; they should ideally be co-located (see sidebar, "The Value Of Integrated R&D Sites.") The critical mass threshold of such 'innovation cells' is still a matter of intense debate, but most evidence points towards 50-100 people at most. An R&D site can then consist of a number of such 'innovation cells' but should also not be too large (500-700 seems a good size, based on our conversations with R&D leaders). Other elements of the value chain greatly benefit from economies of scale such as medicinal chemistry or enabling technologies. But especially with the latter, there is a risk of becoming too detached from the core disease biology knowledge creation process.

**6. Last but not least, do we have a flexible model that enables a high degree of internal and external collaboration?** It has become standard practice to integrate internal and external assets and capabilities (ca. 50% of pipeline assets from top 30 pharma companies are either in-licensed or acquired), but finding the appropriate model to do so is tricky. Companies should not be guided by fixed percentages (not even when they are flagged as 'best practice'), but rather be guided by opportunities in areas in which a strong ability to spot attractive projects already exists.

Those executive teams that attempt to answer these questions before a period of hyper-growth really kicks in stand a good chance of building a highly competitive and sustainable model. J&J, BMS and Novartis have demonstrated that it can be done. Ultimately most R&D leaders of strong performing companies know in their hearts that leadership, people and culture are just as important if not more important for success than assets and technologies. **IV**

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**THE VALUE OF INTEGRATED R&D SITES**

What many high performing R&D organizations also share are fully integrated R&D sites, often in close vicinity to academic hotbeds (Genentech Inc.'s one site model in San Francisco, Novartis AG's NIBR in Boston). Scientific innovation, by and large, requires collaboration, even more so in today's ever more specialized world. Brilliant ideas and insights occur at boundaries, often stimulated by intense discussion with scientists from other fields or even just by off-hand remarks by knowledgeable individuals. It would therefore seem that integrated R&D sites could achieve more success than their globally distributed counterparts.

Academia has several examples of this, one of the most pertinent being the MRC in Cambridge, UK. It has produced 13 Nobel Prize winning scientists and has spun-out innumerable companies from their research. Within the industry, Genentech decided against opening up another R&D site outside of San Francisco for this reason. Therefore, the simple method of facilitating this is geographical co-localization, however it isn't the only method, internal knowledge-brokers could help not only in the transfers of knowledge between geographically disparate sites but also facilitate introductions between scientists and team leaders. The book 'How Breakthroughs Really Happen' by Andrew Hargadon, PhD, discusses many organizational principles that enable breakthrough innovation across industries.

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