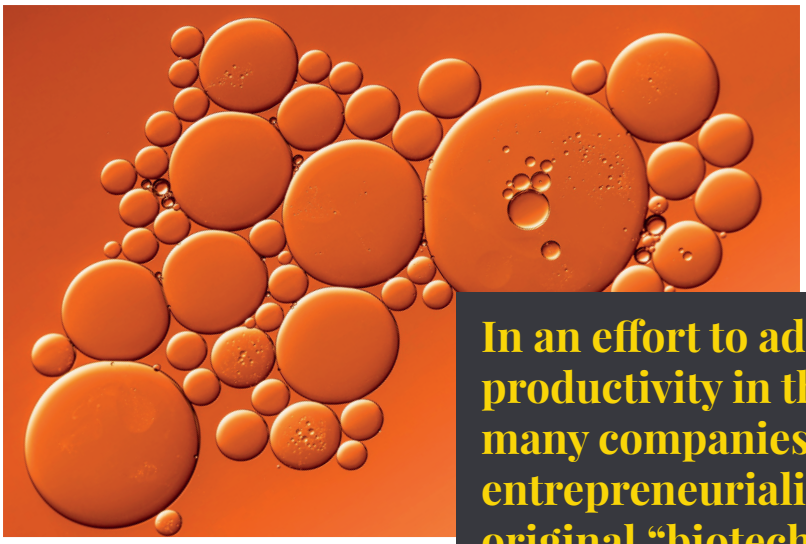
A Biotech-like Mentality in MidPharmas: The Winning Combination?



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In an effort to address declining R&D productivity in the pharmaceutical industry, many companies have looked to the innovative entrepreneurialism that characterised the original "biotech" companies of the 1970's and 80's. This has resulted in numerous restructurings and changes to processes and culture. But what is the real "biotech-like" mentality that the industry is seeking? In this paper we offer our views on what sets the best biotechs apart: focus, flexibility, capital discipline, external oversight, project orientation and culture. We then use a simple, directional set of parameters to assess a group of MidPharmas on these attributes, with some expected and unexpected outcomes and plenty of interesting questions. We offer our views on why MidPharmas provide the ideal environment in which stability and scale can complement the dynamism of the original biotechs, providing a winning combination for long term success.

Introduction

The pharmaceutical industry as we know it today is rooted in the pharmacies, fine chemicals and dye trades of the late 19th century. The following years saw an era of unprecedented growth as the industry pioneers revolutionised the face of medicine and reaped the rewards. The industry agglomerated, benefiting from economies of scale and giving rise

to some of today's Big Pharma. In the 1970's and 80's the breakthroughs in molecular biology and genetic engineering then gave birth to biotechs, causing a splintering of the industry and the biotech bubbles of the 1990's and 2000's.

40 years on from the biotech revolution, we are in the midst of another major turning point for the industry. Despite increased spending on R&D, productivity is down, resulting in extensive introspection and reassessment. In simpler industries, increased scale and process optimisation are enviable attributes because they promote efficiencies. Unfortunately, in the pharmaceutical industry these same attributes appear to stifle innovation.

One solution would be to disaggregate the industry into smaller, "biotech-sized", organisations. Many Big Pharma have adopted this approach, with varying levels of success. Unfortunately structure is only part of the solution, it is mentality and not just size that creates real impact. We see evidence of this among the "grown-up" biotechs, some of which have managed to retain high levels of innovation and productivity despite their large size.

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The innovative entrepreneurialism of the industry pioneers and the early biotechs continue to be an aspiration, and to be more like a biotech has now become an industry mantra. In this paper we therefore discuss the issue of scale and provide our definition of the "biotech-like" mentality. We also use publicly available information to rank European MidPharma on their "biotech-like" attributes.

Is scale inversely related to R&D productivity?

Many analyses have sought to establish whether there is a connection between scale and productivity in pharmaceutical R&D. Unfortunately, long development timelines, high attrition rates and the wide variety of business models make such analyses incredibly complex and challenging. Not surprisingly results have been mixed and inconclusive.

Despite these challenges, we were struck by a recent analysis by Matthew Herper1 that took a very simple approach to the problem. This analysis sought to measure the cost of bringing a new drug to market by taking the total spent on R&D over a ten-year period and dividing this by the number of new drugs launched. This was carried out for 100 companies with striking results. Companies that spent over $20bn on R&D over the period spent a median of $6.3bn per new drug launched (14 companies in total). Those

that spent between $5bn and $20bn on R&D spent just $2.9bn per new drug launched (11 companies in total).

Although such analysis is crude and fraught with pitfalls, these limitations cannot explain the huge difference in cost between the two groups. All of these companies include R&D spend on post marketing safety studies, and all carry the weight of failure in their R&D costs. Bigger companies chasing larger indications may drive some of the difference, but we don't believe that this explains all of the increase. It seems more likely that as companies grow to huge scale, innovation and efficiency in R&D suffer.

Big Pharmas appear to agree that size has limited their productivity and ability to innovate and most have already taken steps to attempt to be more "biotech-like" (Table 1). This has often involved disaggregation of the large R&D organisation into smaller biotech style units.

Table 1. Strategies adopted by Big Pharma to be more "biotech-like".

Company	Acitivity
Pfizer	"Focus on fewer disease areas...less can truly be more, particularly when it forces focus, speed and high quality decisions" (2013)
Sanofi	Closure of R&D sites, reorganisation of scientists to "hubs" to mimic structure and culture of acquired Biotech, Genzyme (2012)
Novartis	Plans to reduce number of R&D sites to consolidate and "co-locate scientific resources" (2013)
Merck	Creation of innovation hubs, recruitment of former head of R&D of Amgen to lead Research, reduction of workforce by 20%, focus on core therapeutic areas (2013)
Roche	Closure of Nutley, USA research site (2012)
GSK	Creation of Discovery Performance Units (DPUs) with internal competition for funding, incentivisation and reduction of red tape (2008)
AstraZeneca	Creation of virtual innovative medicines unit (iMed) for research into CNS, consolidation of global R&D in Cambridge, UK
Johnson & Johnson	Creation of Innovation Centers to foster life science start-ups in biotech and health IT (2011).

Sources: Novasecta analysis of company websites and press releases, ordered by sales 2012.

For smaller companies the solutions are not so obvious. European MidPharmas typically spend between €50m and €1bn on R&D, a small amount relative to the Big Pharmas described above. Yet despite their smaller size, many still lack the innovative entrepreneurialism of true biotechs. Many of these companies represent the vestiges of the old pharmaceutical industry, with similar origins in the pharmacies and fine chemicals trades. Unlike "grown-up" biotechs that had to fight for capital, many are still family owned. Such stability has advantages, for example providing a long-term outlook, but it also creates a sense of comfort that can lead to complacency. For these companies we need to look beyond scale to understand the more fundamental aspects of a "biotech-like" mentality.

What is a biotech-like mentality?

What “biotech-like” means in practical terms is open to interpretation as it is used to denote a multitude of metrics, processes and cultural norms.

When George Scangos, then the CEO of a small biotech Exelixis Inc., was recruited by Biogen Idec to be the new CEO in 2011, he swiftly executed a series of steps to “revitalise” the company and make it “more like a biotech”. Some of the key issues he raised were the limited interactions between employees in large companies, the lack of correct incentives and a risk-averse culture 2.

Frank Douglas 3 identified similar themes when he interviewed 26 former and current leaders of R&D departments at major pharmaceutical and biotechnology companies to discuss entrepreneurship in R&D. This research identified several common themes that limit entrepreneurial behaviour in the R&D departments of large organisations. These included: a focus on “shots-on-goal”; inflexible and bureaucratic R&D groups; homogenised rewards systems; underperforming middle management; and a lack of interaction between R&D Heads and the CEO.

Through extensive experience with European MidPharma companies, Novasecta has identified, in practical terms, the six key attributes that are required to achieve a “biotech-like” mentality in a pharmaceutical company context:

1. Focus.
2. Flexibility.
3. Capital Discipline.
4. External Validation.
5. Project Orientation.
6. Culture.

We describe each of these attributes in turn below:

Focus: Focus in biotechs relates to two aspects: that of focusing on distinctive capabilities, and that of having a focused organisational structure. Biotechs will focus on a single or selected number of activities in order to reinforce and build up a selected set of distinctive capabilities. This allows the biotech to differentiate itself from competitors and also attract the top talent within its chosen area of expertise. Focus also applies to the organisational structure. The co-localisation of employees at a single site creates opportunities for employee mingling, the easy exchange of ideas and an energetic culture formed around a single purpose.

Flexibility: Biotechs consist of lean R&D headcounts with smart balancing of internal and external capabilities. This allows for flexibility around capacity arising from pipeline demands without the burden of large fixed costs or the temptation to “make work” for internal employees. Lean

organisations also generally result in less bureaucracy, greater ownership and the freedom to act entrepreneurially.

Capital Discipline: Often funded by venture capitalist / private equity companies, biotechs must operate extreme capital discipline in order to survive to the next funding round. Not only this, they must ensure the capital spent produces the type of result that will continue to impress the investor community. A "% of sales" is not allocated routinely into R&D and it is not viewed as a "right" by the R&D organisation.

External Validation: The presence of external advisors and investors on the Boards of biotechs brings valuable external viewpoints and expertise. It provides sparring partners for the management, challenging and championing programmes and increasing the value of the final output. This minimises potential impact from promoting pet projects and limited viewpoints, and forces each program to be assessed more objectively.

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Project Orientation: The fate of biotech employees is closely linked to that of projects and the company itself, creating a driver for success. In contrast to function-focused structures found in larger organisations, the internal structures and processes of a biotech are oriented around projects and geared towards supporting progression with a "project is king" mentality. There is a high level of accountability, with an individual with considerable clout usually leading projects and taking ownership of their progress. Further, employees will typically have an equity stake in the company through share options, adding to the sense of "skin in the game" and further promoting a sense of ownership and a desire to push for project success. With increased scale the personal accountability and sense of urgency diminishes and can result in complacency setting in.

Culture: aside from structure and process, the culture of a biotech plays a significant role in its success. This encompasses attitudes stemming from the attributes described above, for example, from a lean structure arises less hierarchy, greater empowerment and decision-making flexibility. The capital discipline means every experiment is significant and project prioritisation becomes paramount, resulting in the direction of resources towards performing the "killer experiments". These rigorous checks coupled

with dispassionate decision-making ensure the fast-cull of assets that do not deliver. This is a stark contrast to resistance to change from "how we have always done R&D" at times found in pharma companies. These aspects, coupled with a can-do attitude are often at the heart of successful biotechs.

How "biotech-like" are European MidPharmas?

Understanding the extent to which a company possesses these attributes requires a detailed exploration of company structure, governance, culture and strategy. This level of analysis is impossible from public sources of information; however, we have identified three directional "biotech-like" parameters that can be assessed from publicly available data:

Deal count: the number of out-licensing deals and joint ventures for internal products per R&D spend over the last five years.
Visibility: newsflow per R&D spend over the last five years.
R&D flexibility: R&D headcount per R&D spend in 2012.
These are classic "biotech-like" behaviours and represent proxies for some of the attributes we describe above. Deal count and visibility both reflect the drive to gain external validation and/or financing through deals and enhanced newsflow. A lower R&D headcount relative to R&D spend suggests increased flexibility and smart balancing of internal and external capabilities. All three parameters have been normalised by R&D spend to account for the wide variation in the companies evaluated.

Using these parameters, we ranked 30 MidPharmas with diverse ownership structures, business models, histories, capabilities and cultures for their "biotech-like" mentality (Table 2). Although it is impossible to draw definitive conclusions from such a crude approach, we believe that the ranking provides plenty of food for thought and raises some important questions for all companies to address.

The high ranking of the top two companies – Denmark-based Genmab and Swiss-based Helsinn – seem to us to represent well the success that comes from a biotech-like mentality. Founded in 1999, Genmab is a quintessential "grown-up" biotech that recently saw its stock price soar due to the progress of flagship oncology products ofatumumab (Arzerra®) and daratumumab, the latter a recipient of the FDA's Breakthrough Therapy Designation. Family-owned Helsinn, with its lean internal structure and an interesting business model that requires in- and out-licensing, has also grown its business strongly and has demonstrated both a strong track record in FDA approvals as well as confidence in its R&D: 32% of sales were invested in R&D in 2011, with an R&D investment CAGR of 23% over the period from 2007-2011.

Table 2: MidPharmas ranked by biotech-like mentality measured from an external perspective.

Company	Deals / €1m R&D Spent (2009 - 2013)	Visibility / €1m R&D Spent (2009-2013)	R&D Heads / €1m R&D Spent (2012)
Helsinn	●	●	●
Genmab	●	◕	●
Sobi	●	◕	◕
Oxford Biomedica	●	●	◑
Active Biotech	◑	●	●
Ablynx	●	●	◔
Recordati	◕	◕	n/a
Symphogen	◑	◕	●
Almirall	◑	◑	●
Morphosys	●	●	○
GW Pharma	◑	●	◔
Ipsen	◔	◑	◕
Vectura	◕	◑	◔
Stallergenes	◕	◕	○
Lundbeck	◔	◑	◕
Zeltia	◑	◕	○
LEO	◔	◔	◕
Chiesi	◑	◔	n/a
Skyepharma	◕	○	◔
UCB	○	○	●
Esteve	◔	◑	◔
Shire	◔	◔	n/a
Grunenthal	○	◑	n/a
Gedeon Richter	◕	◔	○
Orion	◕	○	○
Sevier	○	○	◕
Galderma	◔	○	n/a
Actelion	○	◔	◔
Merz	○	○	n/a
Pierre Fabre	○	◔	○

Key: ● Favourable ○ Unfavourable

Sources:Novasecta analysis of Medtrack, company websites and annual reports.
Notes: 30 selected revenue-generating MidPharmas (2012 revenues below €4bn) were analysed on three parameters as proxies for a biotech-like mentality. The companies were ranked on each parameter independently, and aggregated to provide the final score. Deals analysis was based on Medtrack data on Partnership deals within the last five years where company

of interest was listed as Target/Source company. The number of out-licenses for products (each product included once) and joint ventures were counted from this. Visibility was measured through a manual count of the number of press releases (excluding regulated releases) over the last five years. Number of deals and newsflow over the five years was normalised to the total R&D spend over a five-year period. R&D headcount data was taken from company websites and annual reports where publicly disclosed. For the total ranking a median R&D headcount / €1m R&D in 2012 spend was allocated to companies where figures were not available for ranking purposes (marked as n/a in table).

However, other rankings were more unexpected, including those of Shire and Actelion. Low ranked on our parameters, UK-based Shire is well regarded by the markets and continued growth in R&D investment (15% CAGR, 2007-2012). However Shire started with a search-and-develop model prior to acquiring and then developing its own R&D, which is not incorporated in our quantitative assessment. Similarly, Swiss biotech Actelion has been a biotech to pharma success story since its founding with ex-Roche assets in 1997, and had a successful 2013 with the FDA approval of Opsumit® (macitentan) for pulmonary arterial hypertension. However it did come under significant investor pressure in 2011, and its revenue growth appears to be slowing down (1% CAGR 2010-2012). We were also surprised to see UK-based Oxford Biomedica being so highly ranked, yet having decreased its R&D investment over the last five years (-12% CAGR, 2007-2012) and having had a share price drop by almost 70% over the last 5 years.

Our simple ranking methodology of course has its flaws. Counting disguises the fact that some deals and press releases (and indeed R&D heads) clearly have more quality and importance than others. Counting the number of outlicensing deals and joint ventures also favours business models that place a strong emphasis on business development and we can only count those deals that are published. We have included deals for developmental as well as commercial products so our normalisation by R&D spend will favour companies with more commercial deals. Although we excluded regulated releases, visibility still favours public companies. However, we believe all companies should strive to do deals with suitable partners and maintain their visibility and communicate value inflection points. Comparing R&D spend and headcount between different companies is complicated by multiple factors including: tax incentives driving R&D cost inflation, differing commitments to post marketing safety studies, different costs per R&D head in different countries, and different classifications of an R&D head. Finally, as all of these parameters are normalised by R&D spend, our ranking favours companies that spend less on R&D.

Despite these limitations, we believe that our ranking demonstrates well the diversity that we experience in MidPharmas in how biotech-like they really are. It also raises some interesting questions. For example, would companies that are ranked low benefit from behaviour that appears to

be more biotech-like to the external world? Would more flexible capacity support their growth ambitions? Could more deals be struck to gain external financing and validation for in house projects? Similarly, are the high ranked companies capitalising enough on their apparently biotech-like behaviours and translating this to increased productivity in terms of both quantity and quality?

Biotech-like mentality in MidPharmas?

While Big Pharma may benefit from being more like biotechs, it is our belief that MidPharmas are better positioned to use biotech-like attributes to their advantage. A difficulty faced by most biotechs is the constant need to raise financing, often putting a strain on management energy and effort. Financial pressures and focus on single asset or technology can also mean that good structure, processes and attitudes are wasted in biotechs.

In MidPharmas, revenue from own sales or royalties, relatively smaller scale, a surviving entrepreneurial spirit and often-family ownership can be combined to provide greater financial stability, amenability to adapt to change and a longer-term outlook. Harnessed properly, this can be the ideal environment for a biotech-like mentality to thrive. While care must be taken to adapt for scale, for example excessively flexible organisations may lose alignment and overly lean structures may lose critical mass, the best aspects of biotechs and MidPharmas can be leveraged to build highly efficient organisations. Some MidPharmas may already appear to be in possession of biotech-like attributes, however, as our ranking shows, the key is using these for greater output. Therefore MidPharmas should explore how to apply the attributes in their own unique contexts, and then drive the changes required to do this. The answer to industry's constant search for R&D efficiency and productivity may lie in combining the ambition and stability of such MidPharmas with the mentality of the original biotechs.