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SECTOR ANALYSIS

Global biopharma between stagnation and outperformance

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Looking at the market appreciation of biopharmaceutical companies during the last 2-3 years (biopharma share index, IPOs, funding flows) it is clear that this industry is back in the spotlight of investors. While the MSCI pharma/biotech index had risen some 100 percent from 1996 to 2011, it has added another 240 percent (+340 percent since 1996) in just the last four years.

But at the same time, some people are concerned about the recent trend not being sustainable and this year's setback of the MSCI pharma/biotech index dropping to 'only' +300 percent since 1996 could be viewed as a signal that it was all a flash in the pan. In fact, memories of the last bull market around the 'genomics hype' of 2000 come to mind. At that time it all ended in a crash when the bubble burst. The following decade of productivity crisis saw rapidly increasing R&D budgets, stagnating or decreasing output in terms of novel drugs – a condition that afflicted mostly large or big pharma companies, which increasingly relied on M&A, cost cutting and external sources of innovation to survive.

So what is different this time around? This article illustrates some of the underlying causes of stagnation until 2011, the pitfalls some companies ran into and common



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traits among current top performers. Further dynamics are unfolding and we will anticipate a few drivers going forward.

Recent challenges and changes in biopharma

Productivity crisis. Let's face a brutal fact: only an average of 10 percent of drug projects that start the long journey through clinical phases I to III eventually reach the market. While R&D success rates and industry output (approved drugs) have been fairly stable since the 1950s, R&D costs have risen for several reasons: the low hanging fruits have been picked, existing drugs set benefit-risk standards for new ones, and routine biomolecular and medical drug-testing has intensified immensely in technical effort, expertise required and hence cost. As such, R&D costs per new drug have risen to as much as \$2.5bn (which includes all the failures a company has to finance too). For some big pharma companies, that figure can be as high as \$5-10bn. One does not have to be a biopharma R&D expert to realise that the industry is not sustainable at that level.

Partnerships. In response to the productivity crisis, pharma companies have embraced the exchange of intellectual property, R&D expertise,

market power and resources in deal types like co-development, technology alliances and therapeutic area partnerships bridging pharma, biotech and academia. Risk and return are typically shared through upfront and milestone payments plus royalties on sales of the joint project. Over the last decade the business model of many biopharma companies has completely changed from mostly inward-focused to open innovation, where some 50 percent of pipelines within the top 30 companies stem from external sources. Some companies do not even invest into internal research at all (so called search & develop models).

Technical advances. The completion of the human genome sequence set off a hype in the late 1990s and many people believed the solution to most chronic diseases was only a decade away. However, the idea of identifying new drug targets by mere genomics (and validating them later) did not remedy the productivity crisis: the attempt to industrialise pharma research had failed. From the early 2000s, novel modalities (molecule types and concepts such as antisense, RNA based drugs and therapeutic vaccines, to name a few) devised in academia were picked up by the matured biotech industry and pursued by pharma with various

degrees of success. Breakthrough stories like monoclonal antibodies that go back to Nobel Prize winning work in the early 1970s have remained rare, although several promising candidates have emerged.

Drug prices. What is an appropriate price for a given benefit of a drug? In the past, demonstration of safety and efficacy (versus placebo or via indirect comparison with other drugs) used to suffice to obtain market authorisation and almost equalled a green flag for whatever price the drug manufacturer demanded. Since the early 2000s, pharmaceutical companies face new hurdles and tough negotiations on the road to reimbursement. Health Technology Assessment (HTA) has become routine, especially in Europe, and drug makers have to present data supporting their claims of added benefits compared to established drugs before reimbursement categories are set. Consequently, companies now have to include direct comparisons to competitor drugs in their clinical trials to generate these data. Yet implications start much earlier, as companies have to shift the balance of their R&D portfolios from incremental innovation toward more potential breakthrough innovation, which means they now have to embrace and accept much higher risks.

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Recent outperformers

In the above dynamics, several companies have demonstrated that exceptional productivity and growth are still possible. Our recent study on R&D productivity and corporate growth – based on net present value created per R&D budget – of the top 30 public biopharmaceutical companies ranked Gilead, Celgene and Biogen as the top performers in both dimensions. Common traits identified included: (i) a strong focus on specialty disease areas such as oncology or auto-immune disease; (ii) strong internal R&D capabilities, complemented by focused partnering and in-licensing activities; (iii) a sweet spot in terms of size of R&D budgets of €1bn to €2bn; and (iv) a strong science-driven culture and leadership team. The majority of classical big pharma ranks toward the bottom of the list, illustrating a major problem in an industry that still likes to revert to M&A as the solution for many problems: the fact that there are dis-economies of scale within R&D. This makes large companies especially vulnerable to productivity problems that are often further accelerated by mega mergers.

The big question for the current crop of outperformers is whether they can scale up the model that made them successful in the first place. Can a

Biogen or Gilead maintain the pace and keep the organisation both creative and productive as it goes through a period of hyper-growth, or will it inevitably turn into a big pharma and revert to M&A to buy some time?

The promise of novel technology

Further significant changes are expected from technical developments. Some present new challenges for biopharma while others bear a huge potential for value creation that will propel current and future outperformers. We can only highlight a few of the many technological advances that promise to address significant clinical unmet need over the next 5-10 years.

Immuno-oncology is currently the hottest area within biopharma. The idea is to unleash a patient's own immune system to specifically attack tumour cells. This has led to spectacular results in some tumour types and has caught the imagination of the investment community, with megadeals announced and new companies popping up almost weekly. The concept has the potential to revolutionise therapy regimens across many cancer types and a large number of combination trials of immune-oncological drugs with other cancer agents are already planned. Significant benefits in survival for cancer patients

come with significant prices, even higher in drug combinations. Payers already indicate that the healthcare system's budget cannot sustain these price levels, yet the benefits already emerging provide strong arguments for reimbursement.

Cell therapies have immense potential and will one day replace lost or damaged tissues and reconstitute their function. While regrowing Langerhans cells of the pancreas (which produce insulin) has not been accomplished to date, the implications for diabetes would be tremendous. Other tissues like cartilage can already be grown in a petri dish, grown on a matrix and re-implanted at the site of damage to a knee joint.

To conclude, the global biopharma industry is back for good, indicated by the rise in the MSCI pharma/biotech index, and there are many good years to come. Of course, not everybody will gain. The field is competitive and many companies' technologies will be rendered obsolete – which is in the best spirit of Schumpeter's creative destruction – and it is patients and healthcare systems who stand to gain the most. It is the most exciting time in decades to be part of the global biopharma industry. ■