

# Adaptation to the New Industry Landscape

**Independent Consultant Emile Bellott looks at the changing biotech landscape in light of the global financial crisis, and weighs the strategies and options of the players as they seek to reposition themselves in order to create value out of the downturn**

The pharmaceutical and biotech sectors are in the midst of unprecedented and disruptive change. The industry is straining to adjust to the economic and competitive forces at work in the global environment. The success formula for value creation and sustainable economic and competitive advantage is being redefined by an evolving understanding of the global marketplace and industry landscape. Although the current economic recession is at the forefront of public discourse, it is only one of many factors defining the status of the industry. This article describes some examples of how industry players are using strategic choices to best position their organisations for future success, as they emerge from the disruptions resulting from current events.

By early 2009, the serious nature of the worldwide financial recession was coming into focus. Governments of the developed world and of the larger developing countries had all taken steps, through fiscal and monetary policy, to stimulate economic activity and shore up unstable elements of the world financial system. In the first quarter of 2009, the GDP of major world economies continued to slow down.

The pharmaceutical and biotech sectors had always been considered ‘recession-proof’. However, by the first quarter of 2009, industry growth predictions had been pushed back. Economists were seeing slower global revenue growth overall – two to three per cent in 2009 and beyond. The largest components of growth continued to be from developing countries. Developed countries are expected to lag behind: in 2009, first-quarter branded pharmaceutical sales actually decreased by one per cent in the US (1). Combined annual sales of the world’s top 13 drug companies were down by about one per cent. Unexpected consumer pushback resulted in a decline in consumer healthcare expenditure, in response to economic circumstances (2).

2008 was a year of cautious retrenchment in the industry. Larger revenue-producing companies were positioning for cost reduction and strategic realignment. Smaller companies were managing their dwindling cash and looking for sources of capital to sustain business operations. Following a spate of high-profile, high-value mergers, most of the larger players arrived at a corporate structure with both small molecule and biologics capabilities. Biologics represent a higher growth market segment, which is more profitable, and they are less susceptible to competition. At the same time, the revenue-producing companies were poised to build up external pipeline programmes by licensing, partnering and acquisition of smaller development-stage companies on more favourable terms than previously.

## ANTICIPATING THE UNEXPECTED

Previous articles in *EBR* have reviewed the elements of the biotech and pharmaceutical landscapes affecting industry

dynamics and competitive position of the players in 2009 (3,4). The key strategic dimensions of this economic space correspond to policy levers and business strategy options, which provide opportunities to prosper and to gain competitive advantage (5).

In recent research, Lynda Applegate, of the Harvard Business School, showed that disruptions in the economic and competitive business environment present an opportunity to identify and implement value-creating innovations (6,7). Successful organisations do so by identifying the areas they can utilise, and focusing their energies on innovations that produce economic value. These innovations are not only physical products, but also valuable intangible assets, like intellectual property, business practices, alliances and trade secrets. Addressing the sticking points in their current environment opens up opportunities to build an enterprise, product, or business system that is more responsive to the environment and that creates sustained value.

## CAPITALISING ON THE INEVITABLE

*A Book of Five Rings*, by Miyamoto Musashi – a 17th century Japanese martial arts classic – enjoyed a period of intense popularity in the 1980s as a meta-treatise on business strategy (8). Indeed, the spectre of worldwide competition in manufacturing and quality enhanced the mystical stature of this book, which became a bestseller. The book’s key lesson is to view the pitched battle with a worthy adversary – beyond swordsmanship – as a metaphor for business strategy in a turbulent and chaotic business environment. In order to follow Applegate’s formula for building enterprise value out of chaos, we must perceive and take advantage of unexpected circumstances, use policy and strategy levers to our advantage, and to act appropriately to the industry landscape.

These prescriptions suggest that, in maximising value creation and competitive advantage in the current business environment, rational economic actors will do best to seek out the areas that provide maximum leverage for value creation – in Applegate’s parlance, ‘the areas of pain’ – and act strategically. Successful competitors exercise multiple strategy options simultaneously.

## INDUSTRY CONSOLIDATION

A trend towards consolidation is the mark of an industry where there is high competitive, financial, or operating leverage. Over time, the players seek to gain ground against their competitors and gain the advantages of size and market share; an individual competitor can perhaps attain above-average revenue growth through consolidation. The pharmaceutical and biotech sectors are no different in this regard, and follow in the footsteps of many other industries, such as automotive, aerospace, airlines, regional hospital chains and financial services.

The past decade has witnessed a continuous string of large mergers and acquisition deals between pharmaceutical and biotech companies. During 2008, the top 10 mergers assimilated \$79 billion of market capitalisation. In early 2009, additional high-profile mergers have been announced (such as Merck – Schering-Plough, Roche – Genentech and Pfizer – Wyeth), with more anticipated (9). Speculation for the months ahead centres on Lilly, BMS, J&J and AstraZeneca.

Due to the factors that characterise the industry landscape, merging with or acquiring other players satisfies the need for growth and renewal. In the pharma and biotech industries, there is a high cost to sustaining product innovation and an insatiable desire for returns to the sources of capital (10). At the same time, new product opportunities and therapeutic modalities are fueled by the rapid pace of scientific discoveries. Finally, as a measure of cost sensitivity in the marketplace, product exclusivity fades rapidly, following the expiry of patent protection. Most analysts believe that the consolidation trend will continue for the near future, as the remaining mid-tier players move up and a few remaining pharmaceutical companies seek to secure a capability in biologicals and other new revenue-generating products.

#### **M&A AND THE CAPITAL SHORTFALL**

Revenue-producing companies enjoy adequate, if higher-priced, access to capital and adequate cash reserves. They are poised to build up external pipeline programmes by licensing, partnering, and the acquisition of smaller development-stage companies on more favourable terms than previously.

Conversely, early stage companies, whose primary source of revenue has been investment capital, are experiencing extreme financial distress. In many cases, their best option to advance their programmes is to seek partnering or acquisition. In the present financial environment, additional rounds of direct equity investment are more difficult to secure on favourable terms. IPO as an exit strategy is effectively cut off.

In relation to competitive positioning, the financial crisis is a game-changing event, as illustrated by the following factors:

- The lower valuations of emerging company assets may lead to a short-term external pipeline boom (within large pharma) through mergers and acquisitions
- The potential exists for a medium term external pipeline drought
- Emerging and nascent enterprises are most vulnerable, due to capital shortfall
- There is an urgent need to address the 'valley of death' problem and advance early stage and academic programmes up to a minimum value creation threshold (4)

Recent reports assert that 30 per cent of public biotech companies have less than six months worth of cash on hand. Fifty per cent have less than a year remaining. Although figures

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are not generally available for private companies, the situation is believed to be equally grim. (11)

## **COST CONTROL**

Cost cutting is a prudent policy, dictated by the economic environment and industry dynamics. There is intense commercial competition amongst the innovator pharmaceutical companies themselves, as well as with generic drug manufacturers. This pressure has only intensified as these enterprises seek to control expenses, in anticipation of increasing drug pricing constraints within the healthcare reform regime. The American debate and legislative remedies are the most visible manifestation of a worldwide trend towards controlling the escalating and unsustainable costs of healthcare in general. This policy discussion has greater importance for the innovator pharmaceutical companies, since the US market represents almost half of worldwide pharmaceutical drug sales and has been at the frontier during decades of *laissez-faire* product pricing.

The developing world is, and will remain, the area of greatest growth for pharmaceutical drug sales. Over the next five years, drug sales in China and India will sustain a double digit growth rate (1). Despite the advances that these countries have made in standards of living, healthcare affordability is still an issue. Even with indigenous manufacturing capability, the cost of goods will be key. Of course, this does not even begin to address the problems of cost structure in the least developed areas of the world, such as Africa, where there is a great unmet medical need.

Controlling costs goes hand in hand with strategic consequences. The quality of the strategy and execution can set the stage for competitive advantage in the future as the economy rebounds. A false move in this regard can cost dearly in lost future potential. It is not about 'hunkering down', but about being proactive and strategic. In the future, constraints on product pricing will not go away, they will only intensify.

Amongst the large players, several areas of cost reduction have gained traction. Chief amongst these are:

- Reductions in in-house R&D
- Divesting manufacturing facilities
- Reducing medical sales forces.

These three, in particular, would seem to be at odds with the very concept of a 'fully integrated innovator pharmaceutical company'. Indeed, they represent significant changes from the traditional business model. Paradoxically, such adjustments will position these enterprises for the coming decade.

As an example, reduction in in-house R&D is a non-traditional approach to address a number of issues associated with the competitive environment. In analyst briefings, most of the large pharma companies have expressed an externalisation target of approximately 50 per cent of the R&D pipeline. The benefits of this approach include:

- Tapping multiple external sources of innovation in universities and emerging companies

- Acceleration of early development to preserve patent life; greater capital efficiency in early development
- The ability to redirect resources quickly
- Transferring development risk to upstream partners

An added bonus is the opportunity to have a much larger span of early pipeline opportunities, particularly in new therapeutic targets and modalities. From the emerging company perspective, the wave of licensing, partnering and acquisitions provides some relief from the capital shortfall, and an alternative to IPO as an exit strategy.

Reduction of manufacturing assets by outsourcing is more obvious. In the global business environment, there are ample opportunities for outsourcing the production of active pharmaceutical ingredients according to internationally harmonised quality standards. However, proliferation of multiple manufacturing sites, often in remote locales, creates new issues of risk management, and a greater, as yet unfulfilled burden for pharmaceutical regulatory authorities. For example, there is at least a decade-long backlog of foreign manufacturing sites that require audit and oversight by the FDA (12). This regulatory backlog and the urgent need to speed up the drug approval process are part of the motivation for the proposed 19 per cent increase in the FDA budget. The number seems small and perhaps is only a down payment on the needed expansion of FDA staffing.

Manufacturing outsourcing as a strategic option also opens up new marketing opportunities for pharmaceutical companies in emerging markets. It simultaneously transfers the technology and employment base to the countries paying for and consuming the medicines. For pharma and biotech companies, there is an explicit cost reduction opportunity in lower labour cost areas, as well as potential tax advantages.

## **PRODUCT STRATEGY OPTIONS**

Yesterday's pharma business model emphasised development of 'blockbuster' drugs (achieving at least \$1 billion in annual sales). Today, the emphasis has shifted to drugs targeting smaller niche indications in the order of \$100 million annual sales. This speeds time-to-market and preserves more patent life after approval. However, it requires that costs be controlled judiciously, to assure that development expenses are recovered before the drug goes off patent. This in turn places renewed emphasis on Six Sigma techniques, project management and, in the case of shared resources, multi-project optimisation of operations.

With small niche products and the treatment of chronic indications, the healthcare focus becomes prediction, prevention and personalisation. This is enabled by reliance on genomics and diagnostics for clinical trials, and as an adjunct to therapeutics. Several recent high-profile discoveries emphasise the importance of matching the medicine to the patient genotype, in order to identify responders versus non-responders. Use of pharmacogenomics in this way offers the chance to make considerable savings on the cost of powering clinical trials.

Generic competition is intensifying for small molecule drugs going off patent. It is estimated that approximately \$24 billion of

branded drug revenue will lose patent protection in 2009. About \$10 billion went off patent in 2008. Under healthcare reform, industry observers anticipate that generics will only gain in prominence. They will be mandated wherever possible, placing innovative branded drugs in competition with older generic medications. Generics presently represent 64 per cent of drug sales in the US (13). The rapidity with which generics follow innovative small molecule drugs means that manufacturers cannot rely on a long tail for profitability or recovery of development costs. They must therefore ensure flawless and timely execution of their programme plans.

In developing new drugs for the future, the new mantra is not just 'approvable' but 'reimbursable'. Therefore industry criteria for new programmes emphasises unmet medical needs, first in class, and novel mechanism of action.

### THE VALLEY OF DEATH

The timeline from discovery through proof of concept in man, is aptly named the 'valley of death', because this part of the programme is the most risky element of drug development. In the prevailing view of drug discovery and development, the economic value of a programme (pipeline asset) increases over time, as the programme is 'de-risked'. A favourable value proposition sets the stage for monetising the asset, through licensing, partnering or sale. In the classic large company business model, this would not be a problem, as planned and measured resources are applied to meet specified milestones.

The most severe consequence of the current economic recession, with respect to the biotech and pharma landscapes, is the availability of risk capital to fund start-ups and early-stage programmes within emerging companies. During this economic crisis, most of the traditional private sources have shifted their focus toward later stage and less risky investment opportunities.

Overall, the investment in emerging companies has decreased after reaching a maximum in 2007. Total equity investment in life science companies was \$16 billion in 2008 versus \$30 billion in 2007. Venture capital (VC) life science investment was \$6 billion in 2008 versus \$7.5 billion in 2007. VC investment in biotech further decreased by 47 per cent in the first quarter of 2009 compared to the first quarter of 2008 (14-16).

The greater part of the innovations that will ultimately become therapeutic drugs and life saving treatments, originate in academic research institutions. This is because the fundamental research driving the discovery of targets and biological pathways is concentrated in the hands of principal investigators (PIs) at research universities and teaching hospitals.

For the collective life sciences business sector, the greatest potential hazard is not getting innovations from the lab bench through the 'valley of death' to commercial exploitation.

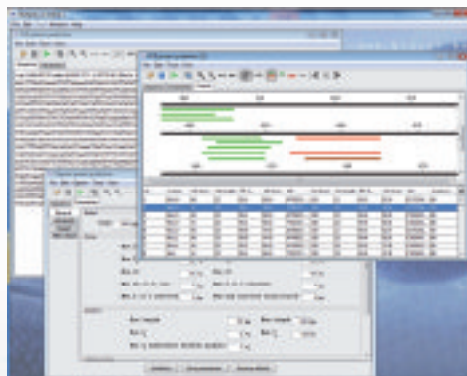
In a tight capital environment and with industry focus on relatively de-risked programmes, the 'valley of death' has become a problem for academic innovators. University technology transfer

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offices have emphasised proactive business development, to appeal to potential interested partners, for licensing and development. They expect to see additional animal data, market projections, and a solid IP position, with freedom to operate.

Major research universities and teaching hospitals have responded strategically, by creating 'accelerator funds'. These funds award competitive translational grants to principal investigators, to help advance their programme towards its commercial potential. In a typical scenario, the technology office provides mentorship, expert advisors, programme planning and other advice, as well as support in contracting and project management activities. To emphasise the speed and capital efficiency of the programme, about two thirds of the accelerator budget would be spent externally with CROs and other industry-savvy outsource partners (17). Reflecting the new realities of the competitive environment, selection of candidate programmes follows priorities similar to those that an innovator drug company would employ. Projects must show a clear path to market and estimation of commercial potential, if successful.

Universities are attempting to utilise other non-dilutive sources of funds, such as targeted philanthropy and government small business grants, whenever possible in support of the acceleration effort. Fortunately, the recent fiscal stimulus bill from Washington provides a \$10 billion increase in NIH funding and additional funds for translational research activities.

The large innovator drug companies are also taking direct steps to address the 'valley of death' problem by establishing funds, with other external investors, to capitalise a portfolio of microventures in therapeutic areas of interest to the pharma general partner. The basic operating philosophy of the fund would emphasise a lean virtual business model, for speed and cost control.

## CONCLUSION

The disruptions caused by the financial recession have accelerated the pace of adaptation within the global business environment. The crisis started out defining the haves and have-nots among the industry players. The ability to deal strategically with the new realities on the ground is defining their future potential for competitive advantage.

### About the author



Dr Emile Bellott is a private consultant in drug development, based in the Boston area. With over 25 years of industry experience, his pharmaceutical activities have focused on drug discovery and development, synthesis and design of small molecule therapeutics, and informatics and structural biology. He has served as VP of Operations, co-founder of two development-stage biotech companies and founder of a life-science software company. His operational experience spans medical devices, pharmaceutical development and chemistry outsourcing. He earned a PhD in Physical Organic Chemistry from Harvard and a MBA from the Harvard Business School. Email: [emile.bellott@gmail.com](mailto:emile.bellott@gmail.com)

In the challenging financing environment of 2009, partnering and M&A will continue to be the preferred exit strategy for smaller cash starved companies. While controlling costs, these small firms will judiciously manage their most promising and most advanced programmes, in preference to the early pipeline.

Large pharma and biotech companies will continue to have unprecedented opportunities to build their external pipelines through partnering and M&A.

The major players will continue the pace of consolidation and merger, to deal with the threat of patent expiry, generic competition, and to gain a foothold in the new land grab in biotech drugs and biosimilars.

2009 will also be a pivotal year for healthcare reform and the opening act of sweeping change in cost containment of healthcare in general and pharmaceutical drugs in particular. This will drive new product strategy and unconventional industry partnerships and collaborations. One example of the latter is the recent announcement by five major pharma and healthcare trade groups to work together with the government in extracting \$2 trillion in cost from the healthcare system over the next decade.

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