Rethinking innovation in pharmaceutical R&D

Ann Baker and Jasween Gill

Date received: 2nd March, 2005

Ann Baker
is a senior executive in Accenture's Health & Life Sciences practice and the Head of Accenture's R&D service line in the UK. Her work in the USA, the Middle East and Europe covers business unit strategy, innovation and R&D effectiveness for pharmaceutical companies. She has also completed several programmes for the UK Department of Trade and Industry, the World Bank and the European Commission, examing the impact of new technologies on industralised nations.

Jasween Gill
Since 2002 Jasween has been responsible for the Drug Discovery Portfolio at CMR International. Using the experience gained while working within Discovery at Pfizer she has collaborated with many international pharmaceutical companies to shape and steer the Drug Discovery Performance Metrics Programme, which assess the productivity and efficiency of Drug Discovery.

Abstract

The pharmaceutical industry is facing a challenge to be productive. One of the solutions to this problem is for the industry to better harness innovation to deliver more and better drugs through the pipeline. But what is innovation and how can it deliver higher performance through more valuable drugs? Historically, pharmaceutical innovation has been seen to be firmly rooted in discovery. The focus has been on the pursuit of first-in-class products based on new targets. However, new research by CMR International and Accenture challenges the view that investment in this type of innovation alone will solve the productivity gap. The research shows that projects based on new targets (no public data are available on the target and no drugs have been developed for it) are slower and less likely to get to market than those based on known targets. (Either some public data are available but the company has not previously worked on the target, or the company has previously worked on and has experience with the target.) Hence, they substantially increase the risk in pharmaceutical research. In addition, there is evidence that later entrants based on known mechanisms and designed specifically to be best in class often displace first-in-class products in the marketplace. Based on these findings and on wider research into what makes high-performing businesses tick, Accenture believes that companies pursuing high performance need to rethink their innovation strategies. Companies must take a broader view of how and where they innovate. Applying novel approaches throughout the organisation and across the entire R&D process may be the true key to higher levels of productivity. Innovation in discovery is clearly important and the portfolio needs to be carefully balanced to maintain risk within acceptable limits and to deliver expected levels of output. But it is not in itself sufficient.

Keywords: *organisational innovation, pipeline challenges, scientific innovation, R&D investments, best-in-class products, first-in-class products, risk management*

Jasween Gill
CMR International,
Novellus Court,
61 South Street,
Epsom,
Surrey KT18 7PX, UK

Tel: +44 (0) 1372 846120
E-mail: jgill@cmr.org

SCIENTIFIC INNOVATION AND RISK

Investing in research on new targets is intended to deliver first-in-class products. However, focusing on new targets greatly increases the risk of failure and extends the time taken to deliver a successful product to market.

Data collected by CMR International[1] indicate that projects based on new targets have significantly lower success rates than those based on established targets in every phase of the discovery process. For example, in assay development, established target projects have a success rate of 76 per cent compared with 57 per cent for new target projects. Overall, only 3 per cent of projects based on new targets are likely to enter preclinical development in comparison with 17 per cent of projects on established targets, according to the CMR International study.

CMR International data also show that projects on new targets typically take 16 months longer to deliver a drug candidate into preclinical development than projects on established targets. The biggest lag is in lead optimisation, which is 17 months longer for new target projects. Lead discovery on the other hand is slightly shorter for new target projects than it is for established targets.

This difference in time may result from new target assays being less well defined, with less stringent criteria than for established targets; established target projects also have higher requirements for demonstrating hits in lead discovery. However, the criteria for entry into

preclinical development are generally the same for both types of projects and the data suggest that new target projects are therefore more likely to dwell longer in the lead optimisation phase than are projects based on established targets.

IMPLICATIONS OF INVESTMENT IN SCIENTIFIC INNOVATION

First-in-class products

Companies that focus large amounts of discovery investment on new targets risk being slower and less successful at getting products into development, and therefore onto the market. Increasing emphasis on productivity means that such companies will need to carefully balance discovery portfolios to manage this risk.

Pipeline challenges

Using the data collected by CMR International on success rates and phase durations for compounds aimed at different types of targets, Accenture modelled a theoretical R&D pipeline. The model assumes a pipeline with a total discovery portfolio of approximately 200 projects and a development success rate of 10 per cent. This model starkly illustrates

R&D investments

the implications of investing in new target research. It shows that to deliver one submission per year, a company focusing exclusively on new targets would need to initiate almost four times as many new

Productivity

projects per year as a company working only on established targets; 90 compared with 25.

Therefore, companies with a fixed capacity must think very carefully about the resource implications of trying to generate a significant number of submissions from new target projects. The

Best-in-class products

resources required to deliver one submission based on a new target could have delivered four times as many submissions had it been based on established targets.

Clearly, a strategy that focuses on new targets, and therefore first-in-class products, risks delivering fewer new drugs to market when compared with an equivalent level of investment in established targets. But does the potential commercial value of these new drugs justify such an approach? In fact, there is considerable evidence that the value gained does not always warrant the investment.

FOCUS ON SCIENTIFIC INNOVATION DOES NOT MEAN GREATER COMMERCIAL SUCCESS

Products that are first in class based upon new targets are not necessarily more successful than products that come second, third or even fourth to market. In fact, there are many cases where first-in-class products have been eclipsed by well-marketed, effectively differentiated follower products. Zantac versus Tagamet is a famous example of second-to-market success based on clinical differentiation, aggressive pricing and marketing. Zantac was priced significantly higher than Tagamet and positioned as the premium product in its class. More recently, Lipitor has been a hugely successful fourth-to-market product. Both of these examples demonstrate the same thing. If a company can articulate sufficient product differentiation and has an effective marketing machine, follower products can deliver equivalent, if not greater, commercial success than first-in-class products.

The number of first-in-class products in the top 10 has steadily fallen over the last ten years. Table 1 shows that the list of the top ten selling pharmaceutical products in 2003 contained just one first-in-class product, compared with seven in 1990. What distinguishes the successful products is that they are designed to be, on some basis, best in class, not first in class. Clearly some first-in-class products, such as Procrit, continue to deliver market-leading performance. But most have shown themselves to be vulnerable to later products that are differentiated on the basis of efficacy, safety or convenience within an existing class of treatment. Such products nearly always result from work on established targets.

Based on these findings, companies that

Table 1: Top ten selling pharmaceutical products in 2003

Rank	2003 sales (US$bn)	Product	Manufacturer	First in class?
1	9.23	Lipitor (atorvastatin)	Pfizer	No
2	5.0	Zocor (simvastatin)	Merck	No
3	4.33	Norvasc/Istin (amlodipine)	Pfizer	No
4	4.28	Zyprexa (olanzapine)	Lilly	No
5	3.98	Procrit/Eprex (epoetin alpha)	J&J	Yes
6	3.63	Advair (fluticasone/salmeterol)	GSK	No
7	3.3	Nexium (esomeprazole)	AstraZeneca	No
8	3.19	Prevacid/Protium (lansoprazole)	Takeda/Abbott	No
9	3.11	Zoloft/Lustral (sertraline)	Pfizer	No
10	3.07	Paxil/Seroxat (paroxetine)	GSK	No

place a significant bet on scientific innovation in discovery could be placing their longer-term performance at risk without the potential benefit of significantly higher sales.

RE-THINKING INNOVATION FOR HIGH PERFORMANCE

Scientific innovation

Consulting

Pharmaceutical companies need to re-think what innovation means in the drive for enhanced productivity and high performance. Scientific innovation in discovery is not sufficient and companies need to examine the possibilities to be innovative in every activity involved in getting a commercially valuable product to market: 'Innovation is not about new targets, it is about successfully bringing to market a product that meets an unmet medical need' (Dr Jan-Anders Kaarlson, Executive VP, Pharma Research, Bayer).

Pharmaceutical R&D

The pharmaceutical industry must focus on innovating throughout the value chain, to differentiate products, meeting the increasing demands of regulators and payers, and accelerating speed to market. Innovation needs to be applied to how processes are designed and refined, how technology is used to enable the business, and how the organisation is structured and people and teams are managed.

Innovative approaches can be used to add value to or differentiate products at multiple points during their transition through the R&D pipeline. This differentiation can be achieved through owning innovative chemical scaffolds, developing new approaches in medicinal chemistry during lead optimisation and later, by creating clinical strategies focused specifically on demonstrating differentiation.

Marketing groups must work closely with R&D from the inception of a new project to its market launch as a drug, to help maintain the focus on creating commercially viable products. Marketing and R&D can work together at the start of discovery, to develop target product profiles. Marketing can also help R&D to understand what is required to differentiate a product in the marketplace.

Companies can also be more innovative in the processes they use to bring drugs to market, and in the organisational structures that support them. Innovative restructuring of R&D processes can enable early and better decision making. For example, companies can adopt a 'proof of concept' model that focuses on rapidly generating the most salient data linked to product success.

Innovation in the later stages of clinical development can greatly improve the transition of products through large-scale trials. New approaches, such as electronic data capture, process re-optimisation and,

more recently, the off-shoring of capabilities such as clinical data management, have all greatly improved the efficiency of trials.

Organisational innovation

Organisational innovations that encourage creativity and the mingling of views across disciplines improve how companies identify winners. Some organisations also advocate keeping 10–20 per cent of resources free to work on ideas that fall outside the defined strategy. Inspirational leadership, a culture of openness, trust and respect for the individual, and a company-wide belief in challenging the paradigm and seeking novelty are seen as vital components by others. After all, if nine out of every ten projects eventually fail, a manager has a much better chance of making the right decision in killing a project rather than keeping it going. While late stage failures are very obvious, incorrect terminations rarely reveal themselves.

Risk management

Strong advocates are vitally important to making innovation successful. They must speak the language of senior management and be both empowered and trusted. In addition, companies need to be careful that the stringent criteria, which are rightly applied to guide decision making do not themselves create barriers to innovation.

WHAT TO DO TOMORROW

Companies need to take two steps to drive productivity through innovation:

- Assess the risk associated with scientific innovation.
- Innovate all the way to market.

Assess the risk associated with scientific innovation

Scientific innovation can create a significant amount of risk in R&D pipelines. While risk is a feature of any R&D effort, it is important that companies understand the level of risk that they can sustain. Different types of companies can accommodate different levels of risk in the pipeline. A small company with only five to ten projects in discovery will be putting its future existence at significant risk if it has a high degree of reliance on projects based on new targets. In contrast, a larger company can sustain a greater number of high-risk projects as long as the overall risk of the pipeline is balanced. The new research presented in this paper enables companies to make more informed decisions about the level of risk resulting from scientific innovation that is acceptable and appropriate for their organisation.

Higher sales

Innovate all the way to market

Companies need to assess how well they currently use innovation to add value to products through every stage of discovery, development and commercial. In doing so, they may identify considerable opportunities to improve productivity and drive product commercial potential.

Any changes in processes and structures need to be supported by a broadening of the culture of innovation beyond the discovery organisation. Every part of the organisation must feel it has a mandate and requirement to innovate. Key to this is empowering individuals and teams to innovate, and providing incentives, as well as rewarding innovation more broadly.

MANAGING RISK, HOLISTIC INNOVATION

In summary, focusing on new target-based research significantly increases the risk, timelines and resource requirements in pharmaceutical R&D. However, it does not necessarily increase the chances of commercial success.

Successful companies will be those that make balanced decisions about the level of risk they are able to manage within their pipeline, and take a holistic approach to innovation. Innovation should no longer be seen as the responsibility of discovery scientists. Successful companies

will embrace innovation at every stage of R&D and marketing, with a clear focus on the delivery of commercially viable products to the market. They will seek to innovate from the earliest stages of discovery all the way to the customer, looking for new ways to add value to the product, make better decisions and speed the process.

Reference

1. URL: http://www.accenture.com/xd/xd.asp?it=enweb&xd=industries%5Chls%5Cpharma%5Cinsights%5Crethinking_innovation.xml