Project acceleration – the case for quantum change

'Hourly sales of $114,000 for a billion-dollar product are a powerful incentive'

The research-based pharmaceutical industry continues to evolve. Business leaders pursue alternative strategies, such as the virtual corporation, and mergers to achieve vertical or horizontal integration, with equal vigor. Discovery programs integrate biotechnology, genomics, molecular diversity, combinatorial chemistry and high-throughput screening as they discover, evaluate and exploit new targets. Development projects cope with the growing expectations of regulators and consumers that increase time and cost.

Much of the new technology applied to the 'discovery' process has the potential to accelerate this initial phase of drug development. Acceleration of the traditional 'development' phase of projects has been announced by many companies; for example, Glaxo (now Glaxo Wellcome) targeted 5–7 years against the 9–12 years taken in late 1994. The real business need, however, is for acceleration of the entire process in order to optimize portfolio size, revenue and life-cycle management.

Many companies have recently discussed their targets for new chemical entities (NCEs) per year. Glaxo Wellcome wishes to introduce three significant new medicines per annum by 2000. Hoechst Marion Roussel (and many other companies) are striving to produce two per year. Even a simplistic modeling of the project portfolios necessary to sustain such output illustrates the importance of time of development. Imagine a target of two NCEs per year, and a success rate of one approved NDA (New Drug Application) for seven compounds entering development. In this case, a company with an average development time of eight years must support 112 projects, while a company that achieves a six-year development time will support 84.

Once approved, the first entry in a new product category is likely to have more regulatory and commercial flexibility than subsequent ones. Both the pace of regulatory approval and the price after regulatory approval are expected to be more favorable for the first compound than for those that follow. The first one or two compounds also have a much better chance to realize blockbuster status than the fifth (or the 10th or 11th). Hourly sales of $114,000 for a billion-dollar product are a powerful incentive to accelerate development by a day ($2.8 million), a week ($20 million) or a quarter ($250 million).

An additional factor that impels accelerated development is the diminishing period of marketing exclusivity. With development taking an average 15 years, as little as five years of exclusivity will remain before patent expiry and potential generic competition. This is because GATT legislation has set the patent term at 20 years from filing and, in many cases, patents are filed before a compound enters development.

Extended exclusivity may still be possible through legislative intervention (such as the Hatch/Waxman 'Drug Price Competition and Patent Term Restoration' act of 1984). Patent protection of critical process or product attributes may provide an additional period free from generic competition. A second polymorph or hydrate, encountered after the initial composition-of-matter patent is filed, can offer additional exclusivity if it confers superior properties. The inability of generic competitors to match complex pharmacokinetic and bioavailability parameters may also lead to additional exclusivity.

Exclusivity in the compound class, however, can be limited to a few years. ER Squibb & Sons discovered the first angiotensin-converting enzyme (ACE) inhibitors, and marketed captopril in 1981. Merck's enalapril was the second ACE inhibitor to reach the US market place, 4 years and 8 months later. Captopril reached $1 billion in sales before enalapril, but enalapril eventually overtook it. HMG Co-A reductase inhibitors and H_2 antagonists are two other compound classes that produced blockbuster drugs for more than one company. The periods of (US) exclusivity for the first entries in these classes, lovastatin and cimetidine, were 50 and 70 months, respectively. Given the competitive nature of the resulting market places, 12–24 months more exclusivity would have provided considerable advantage.

Quantum change is possible; the growing importance of time-based competition demands review of the pace and progress of discovery programs, development projects and, most importantly, their interface (where there is significant opportunity for deceleration). At Bristol-Myers Squibb, an initiative to reduce the time to IND (Investigational New Drug) filing has produced remarkable results. From an average time of 35 months in 1994, we have recently filed INDs in 362 and 384 days, respectively, from time of initial synthesis. This has been achieved by integration of the last phase of discovery with the initial phase of development. Such integration will eventually shorten the time from lead generation to drug candidate synthesis, contribute substantially to optimization of the total drug development process, and best serve the shareholders and customers of our industry.

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