Biotechnology's future and the art of managing R&D

Small, sharply focused biotechnology companies will have an edge in discovery and development.

Viren Mehta

The pharmaceutical industry is undergoing a significant transformation. Multiple forces are changing the face of healthcare. Despite these changes, I believe the fundamental skills needed to succeed in the industry remain unchanged. A company's success will still depend on "R", "D", and "M"—research, development, and marketing. Bioentrepreneurs have an opportunity to take a significant role in this process, but only if they recognize how these three skill sets must evolve, and if they enhance the work of expert managers in R and D. The importance of new therapeutics in healthcare will continue to increase, which in turn will allow selected biotechnology activities to benefit handsomely.

R, D, M fundamentals

Despite my belief that the three critical factors will remain the same, a shift in focus will allow bioentrepreneurs unique opportunities for commercial success. What will emerge is the sophisticated management of these three aspects, especially of Research, which should result in efficiencies never before dreamed of. In the old days—let's say a decade ago—R was unmanageable. The research necessary to discover new drugs was more or less serendipitous, and therefore there was not much to manage. Yes, you needed to find the best people, determine the amount of money you could afford to lose, and encourage the brilliant scientists you hired. But other than that, about all you could do was pray.

Development was driven by this same lack of knowledge. Since the definition of the target the drug was acting on was crude, you could hope for nothing better than the development of a product that treated the symptoms—hopefully without side effects. As a result, regulators dominated the development process. Because their job centered on protecting society, this often became an adversarial relationship. Regulators found that one of the best ways they could do their job was to sit on the data—or worse, ask for more data—until they detected a drug's sometimes-fatal flaw. The process was labor and time intensive, as well as costly.

If you were lucky enough to get past R and D, you finally entered the somewhat familiar territory of marketing products. Not surprisingly, in the old days, it was the marketing people who were kings. They were the people who carried the bag, pounded the pavement, and understood what worked and what did not work, thereby qualifying for the boardroom seats. From their perspective, once the money was in the bank, R and D was not considered a very significant part of the process.

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Drug development's shifting focus

Things began to change in a fundamental way with the advent of recombinant DNA technology. For the first time we got a glimpse of what it means to go beyond the symptomatic understanding of a disease to comprehending disease-causing malfunctions at the molecular level. By comparing how an organism functions normally with what goes wrong when a disease befalls us, we are realizing that what we call a "disease" is really a collection of symptoms that may have a variety of molecular causes.

In the past, we lacked the understanding that one day may allow us to differentiate subcategories of a patient population based on underlying molecular mechanisms. This is why, in the past, drugs that healed many were toxic to some. This kept what could have been important medicines for many off the market because of a few unfortunate patients.

As a result of this understanding, research, for the first time, is becoming manageable. But management of this process is still an art, not something one can learn at a business school. Managing this kind of research requires pioneering instincts because it is likely that the more one fails in this process the greater are one's probabilities of success. This is not the kind of management that lends itself to large bureaucracies and decisions by committee. Rather, it requires small groups of individuals working together toward a common goal. They must be led by someone who can nurture constructive failures and has a knack for knowing when to carry on and when to abandon ship. This is not a strength that everyone can bring to the role of research manager.

Development is also being transformed. The fact that we are now able to start with a known target means that we will also be able to understand how a particular molecule might be influencing that target.

As we achieve a certain critical mass of data, there is a high probability that the role of regulators will change. As molecular pathways become defined and rules for intervention are demonstrated, this body of knowledge will deliver a greater comfort level to those charged with protecting the public. Instead of being adversaries, regulators will increasingly become partners in the drug development scheme, ensuring that the public gets the best drugs in the least amount of time with the greatest safety, and hopefully, at a reasonable cost.

One important byproduct of these changes will be further declines in the product life cycles. International registration of new drugs will become routine. For example, I can envision the day when global phase III studies will be initiated after chip-based evaluation carries a drug through phase II clinical trials. The market forces that currently present economic barriers to developing some of the most innovative therapies will be reduced. This means many more drugs are likely to be aimed at narrower and narrower patient populations because they can be developed cost effectively and command premium pricing. Their lower peak sales potential will be justified by the efficiencies in R&D.

Marketing dethroned

Marketing is similarly poised for a major new paradigm. Just as the financial industry is

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likely to be revolutionized by IPOs through the Internet, so the marketing function will be taken over by the consumer. We have already seen how advertising directly to the consumer has reduced the power of the physician in prescribing drugs. Increasing transparency in the development of drugs and a nearly instantaneous flow of information about a drug's effects are making everyone—not just managed-care buyers—an educated consumer. The implications are clear. Only a real value-added product will have any sustainable acceptance. In the same manner that consumers are now bidding on airline tickets in real time, consumers will ultimately decide the real worth of a therapeutic.

This is a very different business model from what the large pharmaceutical companies need today, as they remember our history of low-tech, low-cost products and aim for the high-tech, low-cost future. While this may sound utopian, the current pace of progress justifies optimism that we may get there in a generation or two. However, this journey from the low-tech, low-cost past to our destiny of a high-tech, low-cost future takes a bell-shaped path, with half-tech, high-cost as the intermediate point on this journey (see Figure 1). As we are probably just coming up to the peak cost structure, the large pharmaceutical companies must knowingly continue to invest heavily in what is currently an inefficient, but will one day become a more efficient R and D process to maintain their position. The synergies resulting from consolidation will provide the cash flow to afford such investments, especially during the dry patches of research productivity.

Biotechnology's critical role

While R, D, and M are being transformed, biotechnology, with its quarter-century of experience in risk management and venture financing, is ideally suited to meet these challenges. The business plans of "research boutiques" justify taking the risk of managing failure that larger organizations rarely can accept.

I expect the biotechnology industry to undergo changes that will enable it to fulfill these critical roles. I expect that only those companies with a proprietary technology that is leading them to exclusive targets or products will remain attractive to both investors and the large pharmaceutical companies. In today's market we can readily identify these companies. When you examine their financial situations they represent the "haves." Companies that sell nonexclusive commodities are also readily identifiable. Today, as in the future, they are likely to represent the "have-nots." They have a role in fulfilling the overflow needs of the larger companies, but otherwise will eke out a meager living.

Because these two categories are already fairly well defined, there have been suggestions that the have-nots should consider merger and acquisition activity in order to obtain the critical mass that would make them favorable candidates as haves. I do not see any logic in this proposal. Three money-losing organizations bound together as one not only quadruples the number of internal problems, but poses nine times the challenge in fund raising. Alternatively, should one of these organizations either have the cash or a proprietary asset it would be diluted to one-third the value.

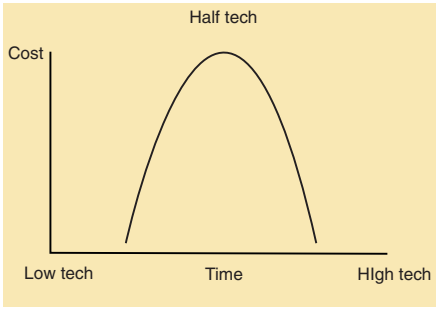

Figure 1. The journey from the low-tech past to a high-tech future.

Smaller biotechnology companies, by definition, lose their creativity and their edge in discovery if they try to imitate the consolidation strategies of the big pharmaceutical companies. While selected complementary consolidation may be beneficial, there is a critical need for small, sharply focused biotechnology companies that can manage the risk associated with the managing of R&D. Because there will be a fair amount of failure before there is success, biotechnology must necessarily be made up of a large number of these organizations. It is likely that not all these companies will succeed. In fact, many will fail. But for every one that fails, new companies will be founded to take on the challenge. Venture capital will continue to fund this innovation process because the winnings will more than repay the losses.

Conclusions

Combining small companies, for whatever reason, is taking them away from their principal strength at a time when this is an overwhelming opportunity. To meet the emerging opportunities head on, new enterprises from the outset must ask themselves two questions. First, "Where is the proprietary interest?" Without an exclusive niche most companies will never be able to prosper, though some may survive. And second, "How can we create an efficient development plan that demonstrates proof of principle?" Companies that can achieve these two goals will produce valuable products that can be sold to a shrinking population of ever-larger pharmaceutical companies. These rewards, in turn, will enable them to go on to the next brilliant possibility. ///