AN AUDIENCE WITH…

Pedro Cuatrecasas

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What do you consider have been the main reasons for mega-mergers of pharmaceutical companies in the past two decades?
Primarily they have been driven by the short-term commercial need to maintain high profitability. The mergers that took place in earlier eras — for example, those that I call the 1980 era mergers — also had an element of strategic value. For example, when the SmithKline Beckman Corporation and the Beecham Group merged (to become SmithKline Beecham (SKB)) and when the Bristol–Myers Company and the Squibb Corporation merged (to become Bristol–Myers Squibb), they attempted to retain the major scientific and product identity of each individual company. Even so, in the case of SKB, the key factor that drove the merger was the decreasing revenue from the Tagamet (cimetidine — the first histamine receptor antagonist to suppress stomach acid secretion) franchise. Importantly, at that time the need to merge was because of product competition, rather than the loss of patents and replacement by generics that have been the universal reasons in the past two decades.

The reasons for recent mega-mergers are straightforward. They relate to decreasing profitability coupled with other factors: first, the loss of patent life, such that sales of major products are cannibalized by cheaper generics; second, the lack of significant products in the pipeline; and third, the corporate cost reductions associated with mergers, as the instant acquisition of products will increase sales and many functions of the acquired company can be eliminated, including R&D and much of the sales force. Acquisitions of the 2000 era are a stark reminder of attempts to reduce costs that resulted in the virtual elimination, in less than a decade, of successful companies, such as UpJohn, Warner–Lambert/Parke Davis and Searle.

In your experience, what effect have mega-mergers had on productivity and innovative research at the companies involved?
The long-term effects are clearly negative. In the short term, increasing revenues do permit R&D to continue but this has unfortunately not translated into increased innovation. I have to stress that the merging of companies has resulted in the loss of excellent established R&D organizations with their high level of manpower, their research programmes and their unique cultures — presumably because these were perceived to be redundant. Instead of trying to assimilate knowledge or learn from the acquired companies, they are simply eliminated, except for their products. This loss of intellectual-knowledge base and specialized staff has had almost incalculably destructive consequences. Then there are numerous complications associated with managing increasingly large bureaucracies. To summarize, the impact on morale, stability, communication and the commitment to long-term scientific programmes has been disruptive. (For an extensive discussion of the issues, see *J. Clin. Invest.* **116**, 2837–2842; 2006).

What key steps do you think are needed to address potential negative effects of mergers?
The only way, in my view, is to not have mergers in the first place! That exposes a crucial dilemma because mergers do offer salvation from declining profits under the current industry system. We have to acknowledge the real problem — the decreasing productivity of R&D. So, what are the basic reasons for this decreased productivity? It comes down to one almost irreconcilable issue: that basic scientific discovery and innovation are simply incompatible with the current organizational structures, management systems and the control of R&D by marketing staff rather than scientific staff. (See *J. Clin. Invest.* article mentioned above).

What would be your recommendations for industry to tackle the decline in productivity?
The industry needs to overhaul or restructure the current system for drug discovery. Today's pharmaceutical companies are dinosaurs. They are anachronisms trying to do today what they did in past eras rather than adapting to the realities of this era. They are still trying to achieve — and are expected to do this by shareholders — extraordinary profits compared with other industries, while being unable to innovate sufficiently. The only viable course for them to ultimately avoid extinction is to focus on the things that they do well and stop trying to do what they cannot do. They need to rid themselves of the self-deception of being the great innovators, dismantle their discovery and early-development organizations, and adopt more realistic profit expectations. They should then focus on acquiring well-defined products for advanced development, developing improved formulations and dosage forms of existing drugs, developing analogues of existing drugs that have superior properties, such as improved pharmacokinetics or increased specificity, as well as manufacturing, distribution, marketing, sales and education — all of the things that they are superb at doing.

What makes such a suggestion realistic is the fact that, during the past several years, in the United States (and other places, but to a lesser extent) there has been an explosion of exciting and productive drug discovery research in universities and non-profit institutions, all under the auspices of federal and state governments, such as the National Institutes of Health. This indicates that the potential for drug innovation in these institutes is enormous, particularly given their culture and organization, which are starkly different from large corporations. When these new discoveries in universities advance in development, possibly through contract research organizations, they could serve as a rich source of potential new drugs for licensing to pharmaceutical companies to fill their development and sales pipelines. This is an area that I am confident will evolve more rapidly than people expect.