Escaping the pincer

An analysis of the past 60 years of pharmaceutical innovation suggests potential strategies to tackle the R&D productivity issues that underlie the latest wave of industry consolidation.

In the last quarter of 2009, the two most recent pharmaceutical company mega-mergers — Pfizer with Wyeth and Merck with Schering–Plough — were completed. Soon after, programmes to reduce the operating expenses of the merged companies began, with Pfizer announcing the closure of 6 of its 20 research sites. The number of associated redundancies for Pfizer and Merck were yet to be finalized at the time of going to press, but were expected to be ~20,000 and ~16,000, respectively, bringing the total number of job cuts by large pharmaceutical companies this year to ~60,000.

One of the underlying factors in these cost-cutting programmes is illustrated in the article on page 927 of this issue, which uses consensus forecasts of the future revenues of 14 large-cap pharmaceutical companies to assess the ability of these companies to tackle the upcoming 'patent cliff' — the loss of revenue due to the introduction of generic competition to many of the industry's most profitable products. The extent of the problem is clearly indicated by the prediction that, between 2010 and 2013, for each dollar of revenue that is lost by the group of companies overall owing to established products going off-patent, only around 25 cents will be replaced by revenue from newer products. Furthermore, the predictions indicate that just six companies among the group have inflation-adjusted operational expenses in 2009–2015 that are sufficiently low for them to maintain their profit margins against a benchmark of 5% compound annual growth rate in revenue, which has historically been achieved by the group overall.

An obvious question raised by these predictions is the extent to which previous mega-mergers have contributed to the failure to increase R&D productivity. Some insights into such questions are provided by the article on page 959 of this issue, which analyses data on the companies that introduced the ~1,200 new drugs approved by the US Food and Drug Administration since 1950. Intriguingly, this analysis shows that the rate of output of new drugs by companies has essentially been constant over the past 60 years, despite the major increases in the level of R&D investment.

The analysis also indicates that companies that have been heavily involved in mergers and acquisitions (M&A) tend to have substantially lower constant rates of new-drug output than those that have not, providing support for the often noted negative effects of M&A on establishing an effective culture of innovation. Nevertheless, even for the most productive large pharmaceutical companies during this 60-year period, which have largely avoided M&A, the rate of drug output is still only about one new drug per year — well below the rate that has historically been considered necessary to sustain company growth.

An interesting implication of a constant rate of new-drug output by individual companies is that one way to increase the output of the industry overall could be to increase the number of companies involved. Again, this goes counter to the surge in M&A activity in recent years, particularly that in which smaller companies have been acquired by large companies, often those that have product-licensing deals with the smaller company. This tendency leads to the removal of an independent potential future supplier of novel products from the marketplace[1]. Indeed, as the article on page 959 notes, although the many small companies involved in drug R&D — of which there are currently estimated to be more than 4,000 — are individually a much less reliable source of new drugs than large companies, collectively they produce more, for less.

The article therefore suggests that a solution to the fundamental industry challenge of improving R&D productivity could lie in organizing innovation networks in such a way that large companies combine their development expertise with the scientific diversity of academic institutions and smaller companies. For example, one proposal[1] for achieving such goals involves moving away from the standard, vertically integrated business model that has been a common feature of drug companies in the past 60 years — and thus perhaps a key limiting factor underlying the observed constant new-drug output. Further investigation of such radical alternatives to established drug R&D models should therefore be emphasized if the industry is to escape the tightening pincer of a constant rate of new-drug output and ever-increasing costs of new drug discovery.

1. Dixon, J. *et al.* Vertical disintegration: a strategy for pharmaceutical businesses in 2009? *Nature Rev. Drug Discov.* **8**, 435 (2009).