nature biotechnology

Realigning interests

Fifteen years after *Nature Biotechnology* was launched, the old paradigms in life science commercialization are no longer tenable. It's time to realign the interests of companies, patients and payors so that innovation is prioritized.

When this journal celebrated its tenth anniversary five years ago, we exhorted the flagship companies to do more to reinvest profits in innovative science and technology. At that time, investors were increasingly unwilling to embrace the risk of early stage research. R&D productivity was in decline. Only a handful of drugs with novel mechanisms were making it to the clinic each year. Today, that situation is even bleaker. Fewer startups are being funded that center around really innovative science. And the types of companies and enterprises that do form are unlikely to be an adequate way of meeting the unprecedented demographic changes and disease burden that will face our societies. If these challenges are to be met, multiple interests must/have to be realigned so that investors and the commercial sector have more incentive to develop novel therapies.

Uncovering new drugs is incredibly difficult. Even if we can address the scientific challenges of understanding human biology, the current investment, regulatory and reimbursement regimes that now govern the sector actively discourage industry from embracing innovation.

From the investment standpoint, the mantra for access to the public markets is now a compound in proof-of-concept trials—a tall order for a company that has plowed substantial resources into developing a drug with a novel mechanism. Both big pharma and, increasingly, big biotech companies are focusing their efforts on satisfying investors via share buyback programs or modifying existing drugs or extending a product franchise to new indications. The risk equation for investing in innovative drug programs simply does not add up.

Even if a company successfully brings an innovative compound through the clinic, regulators continue to raise the quality of data to be gathered in support of an approval, particularly for a novel drug with a novel mechanism. And facing an ever-stretching demand with finite resources, healthcare payors no longer guarantee premiums for innovative new drugs.

At the same time, every stakeholder in the translation process—pharma, government and the research base—has its own diagnosis of the cause of the problem and its own bolt-on solutions.

Pharmaceutical companies want to get closer to the academic and clinical research base both to spot opportunities earlier and to channel them appropriately into their R&D pipelines. But it's hard not to view these initiatives as merely go-faster stripes on the pharma gas-guzzler. When these organizations engage generics companies in pay-for-delay collusions to keep cheaper replacement molecules off the market and axe research jobs by the thousand while only redeploying dozens in academic links, what message does that send about innovation?

As part of his proposed budget for fiscal year 2012, US president Barack Obama has boosted funding for translational research via the US National Institutes of Health (NIH) by some $745 million—a large sum at a time of austerity. The NIH itself has also been taking translational activity seriously. Indeed, NIH director Francis Collins is proposing a specific institute devoted to translation—the National Center for Advancing Translational Sciences.

The flaw in the plan is that the NIH is focused primarily on basic research questions. This is as it should be. But it begs the question as to whether the NIH—or academia for that matter—is well-placed to pick translational winners from basic research. As so many biotech research programs are simply 'parked' because continuation is not commercially supportable, the question is whether the public sector can be oriented to unblock such research areas and reopen commercial avenues.

Fundamentally, then, neither the feeder research programs nor the commercial exploitation machinery is properly aligned with what both regard as the overall driver of healthcare innovation—improving health outcomes. How can the machinery be reoriented to prioritize truly innovative drug development?

Simply providing more funding to venture capitalists in the present environment is unlikely to change the type of science that is funded. Investors will simply fund more of the same ventures rather than those based on truly innovative science. To prioritize investment in the type of science needed to address the healthcare system's disease priorities, such as untreatable cancers, chronic diseases of aging and neurodegeneration or emerging infections, a market pull mechanism is needed to recalibrate the risk equation.

One way this could be accomplished is for government to designate which indications are poorly served through current drugs, represent a burden on the healthcare system and require medical innovation. Incentives could then be offered to companies or institutions that develop experimental drugs addressing these indications.

For example, the US government could co-fund late-stage pivotal clinical research in indications identified as broader health priorities, especially for drugs that have novel mechanisms of action. In doing so, it could both signal its specific priorities and recognize and address the risk in innovation. The extent of government participation could be adjusted according to the order of its healthcare priorities. Alternatively, an increased period of data exclusivity—the time between approval of an innovator drug and the entry onto the market of the same or highly similar product from a competitor—could be offered. The potential returns of five extra years of exclusivity for an innovative drug might make the risk worthwhile, especially if the drug turns out to be a blockbuster.

Government thus has a choice. Keep the alignment in *status quo* and risk a partial or total eclipse of the innovative biomedical enterprise. Or intervene and realign market incentives so that investors and companies can embrace the high risk science needed to develop the medicines of tomorrow.