Unlocking value: John Rountree

How pharma companies can increase R&D productivity

Increasing R&D productivity is a requirement for sustained success and growth in pharmaceutical companies and a pre-requisite for the success of pre-revenue biotech companies.

There is no shortage of analysis describing a decline over time of the industry's R&D productivity. An article by Paul et al in 2010[1] started the trend with an article entitled "How to improve R&D productivity: the pharmaceutical industry's grand challenge." Jack Scannell et al published another article in 2012[2], introducing "Eroom's Law" which refers to the decline in R&D efficiency over six decades from 1950 to 2010. It showed that the number of new drugs approved per billion US dollars spent on R&D had halved roughly every nine years since 1950.

More recent analyses show declines in productivity since then. For example Deloitte's report on measuring the return from pharmaceutical innovation of April 2024[3] described R&D productivity as the change required to reverse the declining trends in returns across the biopharma industry in the past 14 years.

At its simplest, R&D productivity is output divided by input. From a financial perspective, output is the value of new medicines and input is the R&D cost of discovering and developing these medicines. The challenge is that aggregate measures of R&D productivity such as the number of new drugs per billion dollars spent or the internal rate of return on R&D investment are highly sensitive to basic assumptions about how much a drug is worth, the risk associated with developing it, and the significant time it takes for the cost to generate a return. A more practical method is required to address the grand challenge.

Increasing R&D productivity can be achieved by increasing the output and/or reducing the input at an R&D project and portfolio level. The art is to act on the basic drivers of output and input, which for output are the *value* of R&D projects, coupled with the *risk* of their becoming medicines (usually measured by probability of technical success, or PTS), and for input are the *cost* of developing the projects, together with the *time* taken for the projects to reach the market.

These four basic drivers are interconnected, so it is a *system* that discovers and develops great medicines. The behaviour of the system is determined by the people in pharma and biotech companies and how they organise themselves and make decisions.

This year our company, Novasecta, hosted its annual private symposium of pharmaceutical R&D leaders to address the topic of how to improve R&D productivity at a system level. We discussed practical methods to drive R&D productivity improvements through changes to ways of working and operating models, across three topics. They were how to enhance the project-function matrix, how to optimise decision-making and capabilities, and how to blend external and internal innovation.

Enhance the project-function matrix

The project-function matrix is a characteristic organisational form for pharmaceutical companies of all sizes that are developing a portfolio of R&D projects. The project axis of the matrix is designed to create accountability and leadership for each R&D project in a way that brings all the necessary functional expertise to the benefit of the project. The function axis ensures that each piece of functional expertise is nurtured and applied appropriately to every project in the portfolio. There is a deliberate creative tension between the project and function axes. In pre-revenue biotech companies with single assets the matrix is not required, as each function operates solely for the benefit of the single project.

Some pharma companies envy the flexibility of single-product pre-revenue biotechs that operate essentially as effective project teams with everyone focused on the progression of the project. The time-consuming trade-offs and multiple layers of management that are characteristic of pharma companies with portfolios of projects can be seen as disadvantages. Yet if the expertise resident in pharma companies' functions can be applied effectively to individual projects, R&D productivity can be improved.

The project-function matrix alone is simply an organisational structure. To come to life, it must have an associated clarity in *accountabilities and responsibilities*, with *empowerment* of individuals to bring their best expertise and creativity to increase R&D productivity. While accountability and empowerment are easy to say, they are tough to live by. Drug R&D is complex, and the right way to progress each individual project is a matter of judgement, which requires expertise and experience. Yet empowered project leaders and teams may not be as experienced as their more senior colleagues in executive management or individual R&D functions.

Successful pharma companies create and communicate clear visions for each project that enable project leaders and team members to be empowered within clearly defined boundaries. Such empowerment is improved by training, role-modelling and coaching. Measuring progress on these matters and acting on issues are essential tasks for R&D management.

Setting metrics to motivate productivity improvement across the matrix can also drive the behaviour change necessary to make a difference. Simple metrics such as the number of projects to reach typical stages are common. These stages can be the selection of a candidate drug, clinical proof of concept, and first registration. However overly rigid adherence to these metrics can create progression-seeking behaviour where projects of low quality, or value, are progressed in order to meet targets. Accountability is also difficult with such measures, as ultimately project leaders and teams may be motivated to keep low value projects alive rather than stop them and start more valuable project work.

More granular metrics can help, as they can de directly influenced. For example, Pfizer[4] focused on the PTS of its projects through a company-wide initiative that resulted in significant improvements to R&D productivity by increasing the probability that each drug would progress. AstraZeneca[5] created a framework to identify the five most important technical determinants of project success and pipeline quality, which, through application, improved its pipeline quality. In both cases, the metrics were sufficiently short-term to make them meaningful for individuals. They also both aligned with the most difficult productivity improvement metric – output – which is hard to measure financially until many years have passed. By focusing on proxies for the quality and value of what is produced, both Pfizer and AstraZeneca successfully oriented behaviour towards value creation. It is notable that the other side of the productivity equation – input – was not the focus of these initiatives.

Optimise decision-making and capabilities

Sound decision-making at multiple levels and over a long period of time is responsible for every successful medicine, and the lack of it – for the failure of many R&D projects. At a high level in a company, for example, a decision about whether or not to progress a project through a stage – there are usually systems of governance where project teams present analyses to senior-level cross-functional review committees. These committees have the power to decide, or at least to suggest that a decision gets elevated to a more senior committee or board.

While relatively straightforward to set up, decision committees are simply structural frameworks to ensure the right people have good conversations at the right time, informed by relevant data. The art of successful decision-making lies in the practicalities of managing these committees, and making sure that project teams bring creativity, transparency, and strategic options that are worthy of senior-level time. Such ways of working can be encouraged by templates, enforced rules for meeting attendance, and transparency on all relevant data for decision-making.

It is the next layers down of decision-making that can have significant influence on R&D productivity and project progression. These relate to a wide variety of choices ranging from which assays to carry out in the early stages of discovery to clinical protocols, regulatory approaches, and manufacturing methods. These choices can have major implications for both the output (value and PTS) and input (cost, time) sides of the R&D productivity equation. And they require experience and capabilities, both internally and (if necessary) through healthy challenge from external advisors whose interests are aligned with project and portfolio value rather than acceptance by management.

Strong capabilities include both deep functional expertise and the courage to take a decision while accepting the risk of failure. Nurturing and strengthening this entrepreneurial mindset among all R&D decision-makers are core tasks of leadership seeking enhancements to R&D productivity. A further responsibility of leadership is to make sure that if the data (external or internal) does not change, decisions are not re-opened, re-discussed or changed. Such habits create speed and improve project quality, directly increasing R&D productivity.

Blend external and internal innovation

R&D productivity is too important to be left entirely to internal sources or to external innovation alone. So a blend of internal and external innovation has become the norm for R&D operations at most pharmaceutical companies, while there is still plenty of variety in the extent of each type of innovation, and success in making it work. Supplementing internal projects by external projects makes sense for increasing R&D productivity at a portfolio level, simply by increasing the output (value) driver.

It is the way that externally sourced projects are integrated into internal R&D operations that is the ultimate driver of R&D productivity for a pharma company. Ideally, companies create a 'one portfolio' mindset in which each project is assessed on its merits rather than its source, and the measures of value and risk between external assets and internal projects are aligned. Decision-making is kept simple, even though with partnerships there are additional people and layers of governance to consider.

It is the capability to bring in attractive external assets and then progress them effectively that is a core driver of R&D productivity in a blended external/internal model. Such a capability includes top quality internal functional expertise, in order to know what 'good' looks like, and flexible processes to assemble R&D teams, either those standing or ad-hoc, to evaluate in-licensing opportunities. Simple governance without multiple layers also enables the rapid decision-making required to secure assets in a competitive environment.

People, processes, partnerships

It is *people* that discover and develop great medicines, so the first way to enhance R&D productivity is to focus on how people work with each other, how they are motivated, and the mindset that they bring to their work. The people include both internal R&D staff and external partners' staff. R&D productivity therefore starts with the leadership of a company defining and constantly reinforcing both a purpose for R&D and a flexible operating model that enables R&D staff to bring their best to their work. Such an operating model will enhance the project-function matrix, optimise decision-making and capabilities, and blend external and internal innovation.

References:

1. Paul et al: https://www.nature.com/articles/nrd3078
2. Scannell et al: https://www.nature.com/articles/nrd3681
3. Deloitte: https://www2.deloitte.com/us/en/pages/life-sciences-and-health-care/articles/measuring-return-from-pharmaceutical-innovation.html
4. Pfizer: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8719639/
5. AstraZeneca: https://www.nature.com/articles/nrd.2017.244

This article was written by John Rountree, partner, Novasecta Ltd, a specialist pharmaceutical strategy consulting firm.