

IN DRUG DEVELOPMENT, NOT ALL PROJECTS ARE COMPANIES

Delivering innovative, safe and effective drugs has never been so demanding. One way that pharmaceutical companies are meeting this challenge is by increasing their reliance on others to produce new drug candidates. But how well are those other players facing up to the challenge? What changes should the biotechnology companies, their investors and academic institutions be considering if they are to shake off the sector's reputation for low productivity in the discovery and development process?

The pharmaceutical sector is fortunate in that the market demand for effective medicines is growing, and will continue to grow as populations age, and new markets open up in developing countries.¹ Pharmaceutical companies are, however, finding it increasingly difficult to capitalize on this situation and are falling behind in the race to market new medicines. Almost every pharmaceutical executive is all too familiar with the statistics showing the number of approved new drugs (which is declining) compared with the average cost of their development (which is sky-rocketing). This problem, although not new, is caused by the search for treatments to more complex chronic illnesses and greater regulatory hurdles.²

Pharmaceutical companies have been trying to respond to these challenges for a number of years, through mergers, by restructuring R&D activities and by replenishing their development pipelines with innovative therapeutics obtained from the biotechnology sector. This presents an important opportunity for biotech companies, their investors and academic institutions, but they need to evolve to provide the R&D productivity sought by pharmaceutical companies. Big Pharma should continue to excel in late-stage clinical research and marketing, but for this they need the confidence that the other players in the sector can ensure the availability of early-stage assets.

Funding, What Funding?

So what roles do the biotechnology companies, the venture capitalists (VCs) and academia play in the drug discovery and development process and where do some of the problems lie? Venture-backed biotech companies are most often formed on the basis of innovative academic research. Historically, they have taken innovation derived from academic target discovery efforts and conducted investor-funded drug discovery and non-clinical proof-of-concept studies, which has in turn provided a valuable source of validated therapeutic leads for the larger pharmaceutical companies. In



the current climate, pharmaceutical companies are increasingly in-licensing such assets to enrich their own pipelines. Both innovators and biotech companies, therefore, should be optimistic, as the need for validated therapeutic leads is real and growing, in line with the market for novel drugs.

Despite this good news, there are still problems in the European biotechnology industry with biotechs finding it increasingly difficult to attract VC funding primarily because previous investment promises have rarely been delivered and the investors are finding it difficult to raise financing. Add to this the increasing costs and time frames of research and early-stage development. There are many reasons for this, but the most important include the complexity of new biological therapeutics, the focus on chronic diseases, and the requirement by pharmaceutical companies and market analysts for a higher degree of validation before they consider investment.³ As a consequence, there is an increasing gulf between the time taken by the biotechs to achieve a sufficiently mature pipeline for a VC exit (with biotech companies typically having a 6–10-year conception to exit life cycle), and the timeframe of a typical VC investment cycle of 3–6 years.

A Broken Model

As a result of limited funds, VCs are increasingly cautious about their investments, preferring to finance later-stage projects and first-in-class therapeutics that

have a greater chance of attracting pharmaceutical collaborations. This is causing a shortage in funding of early-stage development and a gap between academic target discovery and lead candidate selection. Traditionally, VCs have realized returns on their investments by an Initial Public Offering (IPO) of the funded company on the stock market or a trade sale. The current stock market climate, however, doesn't favour IPOs, which now represent only 1.7% of VC exits as opposed to the 45–50% that was common prior to 2000, leaving trade sales as the most common exit option.⁴ Another impact of limited financing on biotech companies is that multiple projects are often developed sequentially rather than in parallel, limiting pipeline flow and causing internal teams to be underutilized. These circumstances make it difficult to build a diverse, innovative and full development pipeline, which is one of the prerequisites for an exit via an IPO.

The final player is academia, which provides a rich source of innovation through charity and government funding that has often been donated with the aim of improving healthcare. Governments, however, measure academic achievement through their publication records and, unfortunately, the early publication that this encourages can obstruct the development of the innovations into the products that improve patient care. Patents need to be filed prior to publication to safeguard the intellectual property (IP), creating a serious issue for technology transfer offices who then have a limited time to out-license these, often, early-stage projects to fund patent maintenance. This can also devalue the innovation as patent protection is limited to 20 years so early patenting leaves a shorter period of exploitation during which pharmaceutical companies can recuperate their investment.

PROJECTS NEED CHAMPIONS, BUT THESE CHAMPIONS ALSO NEED TO BE REALISTIC ABOUT WHETHER ASSETS ARE WORTHY OF DEVELOPMENT.

Developing a New Paradigm

How can these problems be resolved to increase the flow of innovation from target identification through to the final marketed product? There are three possible broad approaches:

- Alignment of all the players by closing the gap between academic target discovery projects and later stage validated leads. This could be achieved by further advancing drug development programmes prior to the funding of VC biotech companies, to reduce risk.
- Reduce the financial impact of the high risk associated with early-stage development programmes by concentrating resources on developing programmes as assets rather than building biotech companies with their associated infrastructure costs. This is particularly pertinent for VC-funded biotechs developing a single asset, where a virtual model would be a more viable alternative.
- Improve decision making and increase efficiency across the whole research and early development chain by accessing the required expertise through outsourcing.

Mind the Gap

One practical way in which to close the early-stage development gap would be to combine the lead identification and optimization stages of multiple therapeutic programmes within a virtual umbrella structure or 'factory' where they could be advanced to a more viable stage. This could be done within a new type of virtual structure, outside the make-and-break cycle of the biotech industry, with resources used to advance therapeutic assets rather than to build company infrastructure. In this setting, programmes could be evaluated independently and advanced to a stage where investor interest could be gained. This would allow a culture whereby critical experiments could be planned with a 'fail fast' design to reduce the risk, and, therefore, the financial impact, of advancing nonproductive projects.

Projects Not Companies

These virtual structures could be a form of incubator where projects rather than biotech companies could be nurtured. They could be formed within academic institutions or by investors, and would comprise teams of project managers who would advance programmes purely on the projects' scientific and business merit by using the most appropriate outsourcing solutions. In the academic sector, these structures could be funded, in part, from development grants (see sidebar "Other Funding Sources"), but could also in the medium and long term be autofinanced by the revenues generated from successful out-licensing deals. They could be part of the technology transfer offices' remit, facilitating full exploitation of the institutions' innovations.

Other Funding Sources

Research and development grants are available both at national and international levels, and can provide an important source of non-diluting financing for the biotechnology sector. Such grants include European grants (FP7 and EUREKA), together with national grants including UK (TSB, Wellcome), France (OSEO, ANR) and Belgium (IWT). Academia and technology transfer offices could use these grants more effectively to perform development-related activities to advance assets to a stage when they can be spun-out or licensed. Using companies (such as Mint Europe) that are experienced in preparing grant applications and often work for a success fee allows projects to be built with little or no financing and can maximize the chance of a successful application.⁵

Focus on the Asset

Index Ventures has developed an asset-centric approach whereby single assets are purchased from academia and are advanced to key early development milestones using an employed management team with strong project and leadership skills. If the project fails then project managers are recycled to the next project in the pipeline. Each project is, therefore, assessed on its own merit as the project managers are secure in the knowledge that their jobs are safe if their project fails.³

Best Practice in Action

Imperial Innovation, the technology transfer office of Imperial College, London is building a long-term business through a combination of investment financing, incubation and technology transfer activities. During the last 4 years they have invested £48 million from an evergreen fund that does not have the normal 3–6-year investment cycle. In addition, Imperial Innovation provides both project development and business development expertise to their investees.

Some technology transfer offices, including Imperial Innovations in the UK (see sidebar “Best Practice in Action”), are already adopting this model.

Investors could also manage similar structures that allow ‘project incubation.’ The investor would assemble a number of innovative projects and finance their early-stage development using a dedicated team of project managers. Such project incubators would enable multiple projects to be independently evaluated and advanced at minimal costs to the investor, without the need to build a company around each project (at least until key milestones have been reached). This would allow the investor to make a more informed decision concerning each project, thus reducing his or her medium to longer-term investment risk. Moreover, for the investors, this project-driven rather than company-driven approach is highly compatible with the realization of their investment through trade sales, which, unlike IPOs, do not require company infrastructure. These changes are already beginning to appear in the industry and include Index Ventures (see sidebar “Focus on the Asset”), together with a number of virtual biotechs, such as TPP Global Development.

Such ‘project incubation’ could be undertaken without any fixed or infrastructure costs, by using companies that provide outsourcing services specifically tailored to the operational management and advancement of early-stage therapeutic development. These service providers have the experienced personnel in place to rapidly advance programmes and allow maximum flexibility for clients, together with independent quality reporting.

Learn to Fail Fast

Improving decision making is a key factor to increasing efficiency within early-stage development programmes, through accessing experienced development managers, which can often be most efficiently achieved through outsourcing. This allows immediate access to developers who already have proven track records and the ability to offer creative solutions to what may often be considered to be serious hurdles to programme advancement.⁶ Biotech companies could benefit from improved decision making with a ‘fail fast’ design. Currently, this is often not the case as inventors and internal research teams have a vested interest in project continuation. Projects need champions, but these champions also need to be realistic about whether assets are worthy of development. One way to ensure this is to use impartial third parties through outsourcing.

A Virtuous and Virtual New Future?

Much of the biotech, investor and academic sectors are not structured to enable the smooth flow of innovation from target discovery through to clinical-stage



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therapeutics. There are, however, emerging examples of new models that are showing clear signs of success. It is no longer feasible to build potentially unsustainable biotech companies around a single unproven therapeutic, led by scientific founders who have proven track records in academic research, but not in drug development. With money so hard to find, the model based on a single compound, not fully ready for preclinical development, is no longer viable for many investors who are looking for later-stage, safer investments. This is opening a gap between academic target discovery and the industrial development of therapeutics, and new models need to be found that allow the advancement of the project prior to investor backing. Virtual structures that group these innovative therapeutics together to manage their development on a project basis rather than building company infrastructure would be a more efficient and successful route for the industry’s future.

Programmes could be advanced within academia’s technology transfer offices or within umbrella organizations established by investors. Either of these organizations could build internal project management teams or outsource activities to preformed project management service companies. The resulting validated later-stage programmes could then be partnered or bundled into companies to generate further value. There would be fewer biotech company failures if new therapeutic molecules could be advanced further along the drug development pathway prior to the entry of major venture capital. **Pharma**

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