Emerging drug discovery alliance models

The current environment for early-stage drug discovery and development is fluid and the probability of success continues to be challenging.

By Dr Swati Prasad, Mary Louise Bell and Dr Charles McOsker

Advancing an idea from an academic or basic research setting into a therapeutic product that benefits patients is time- and capital-intensive, sometimes inefficient and – frustratingly often – unsuccessful. This reality has led entities in the early drug discovery and development ecosystem to utilise new alliance-based partnership models to increase their chances of success. These new and emerging models come in many flavours, but generally seek to engage resources where they can make the biggest positive contribution and generate productive collaborations. By bolstering communication channels, engineering processes that support the collaboration goals, sharing risk and aligning incentives, these new models have the potential to increase the efficiency and success rate of drug discovery and development.

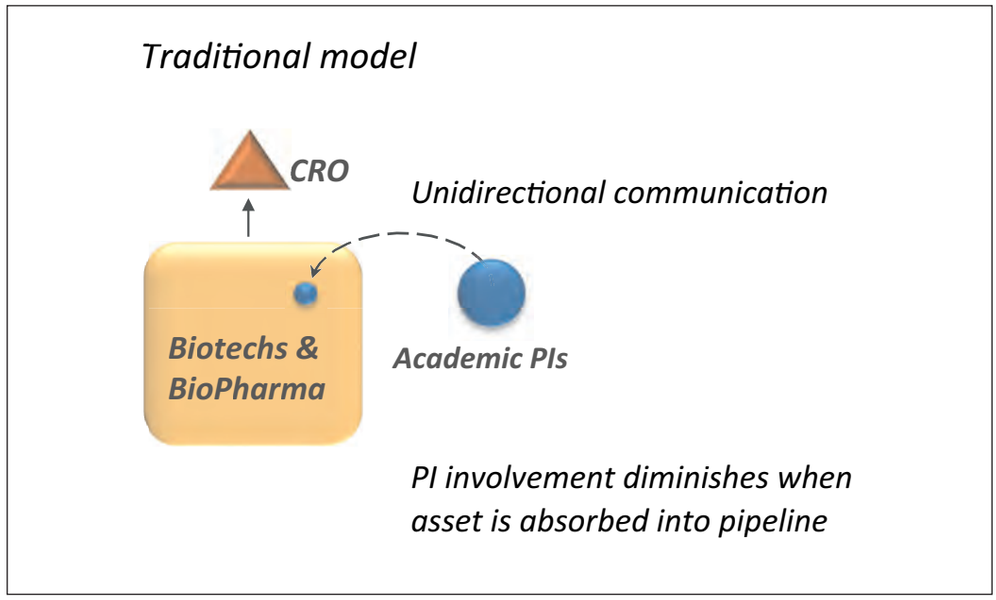
New and emerging alliance models can get a programme to the summit

Success in the drug discovery and development arena is a Sisyphean task. Teams struggle to push a weighty boulder composed of scientific and business challenges, development costs, regulatory requirements and many other elements up a steep mountain of risk to reach the summit. Each one of us may define the summit differently based on our own individual programmes and/or companies, but ultimately the goal is to have a positive impact on the lives of patients by delivering an effective therapy (**Figure 1**).

The early phases of drug discovery, the first three to five years of this process, are often the most perilous, as teams strive to prove out the scientific validity of their ideas and generate proof of principle, usually while operating on a limited budget and struggling to address resource gaps. At the same time, they need to be constantly monitoring medical need and the competitive landscape, and developing business strategy. The ultimate goal of these early studies is to reach a go or no-go decision for further development, while using the least amount of capital possible. Even in the case of a desired outcome, generating the compelling pre-clinical data that is required to capture a strategic partner or deep-pocketed investor's attention – necessary to take the asset to the next level – requires considerable time, expertise, resources and capital. In this effort, non-traditional alliance models and alliance innovation can help overcome obstacles and accelerate progress toward the summit.

Figure 1: Non-traditional alliance models are pathways for overcoming obstacles to commercialising innovation

Figure 2
Traditional model



Innovative alliance models in drug discovery

Most traditional models of drug discovery fall somewhere on an 'inside-out to outside-in' spectrum. At the inside-out end most, if not all, research and development is done internally. Although the entities that employ these models adopt innovations from outside sources. However, these innovations are typically brought into the fold of the company for further development. As illustrated in **Figure 2**, the traditional drug discovery alliance model has been one in which a biopharmaceutical or larger biotech company focuses mostly on internal learning and resources, supplemented by external principal investigators (PIs) and contract research organisations (CROs). The 'not invented here' syndrome, which leads an organisation's culture to reject even the most promising innovations brought in from outside, may prevail in this traditional alliance model.

More recently, with an outside-in approach, central players act as a linchpin or fulcrum at the centre of the effort, connecting innovators to resources and often also developing regulatory and marketing strategies for bringing successful candidates to the market. In this approach, the biopharmaceutical and larger biotech companies invest in external sourcing activities such as licensing, M&A and R&D collaborations. However, these R&D collaborations still tend to be limited to specific needs and niche programmes, and are often one-way relationships that generate data to meet a specific need in a biopharmaceutical pipeline programme. While this approach has helped companies populate their pipelines, it does not make full use of key opportunities that have arisen in the drug discovery and development process.

Much ink has been spilled over which method is best – inside-out, outside-in, or a combination of the two. Passionate arguments have been raised on every side. But in the end the resolution of this debate comes down to a familiar refrain in the management of human institutions: it depends. The carefully calibrated and complex research process that is essential to one programme may be wasteful and unnecessary in another; it is up to the interested parties to make the judgement.

In the last five years, entities in the drug discovery and development ecosystem have experimented with, and engaged in, a wide range of models, including but not limited to: open innovation models, pre-competitive approaches, innovation centres, venture co-creation, build-to-buy and fund-related approaches. The central players involved in these models have not changed much over the years. Large companies generally offer capital and research resources to the process, and academics are most often the original innovators, funded by government agencies such as the National Institutes of Health. At the earliest stages, innovations from academia may receive further public funding or the support of interested non-profits.

These programmes tend to be some of the most efficient, inexpensive and early ideas and experiments that generally are not expected to result in new, marketable drugs right away. They remain

committed to providing science for the sake of science, only indirectly contributing to the drug market by adding valuable data to the sum of knowledge in the field. But once an innovation attracts attention from for-profit organisations, the complexity and cost of drug discovery and development increases exponentially. Here is where ownership of the innovation is apportioned, as well as the dispensation of any eventual profits. However, with less than 10% of drugs from this stage making it to market, organisations and stakeholders involved in the process are required to take on considerable risk. To manage that risk, a number of diverse players in the drug discovery and development ecosystem have emerged and are engaged. Various types and sizes of organisations occupying specialised niches have emerged, including non-profit research organisations, foundations, small and scrappy biotechnology start-ups and contract research organisations (CROs). These entities are often nimble and efficient – able to apply their expertise to a few key functions or to solve a particular set of problems – and with each offering an opportunity to add value to the scientific programme and accelerate scientific assets and programmes forward.

Perhaps the most promising development in this changing landscape is the evolution of CROs. Though CROs have always had a part to play in the drug delivery pipeline, their ability to streamline research has made them even more relevant in today's market. With CRO management structures dedicated solely to execution of research without the distraction of other departments, CROs are able to adapt quickly to the sometimes unexpected demands of new research. Historically, CROs were used for one-off contracts. These relationships were brief and simple, with CROs taking one small part of the research burden away from the larger company and being paid a set fee for their service. This relationship, though useful, no longer realises the full potential of CROs to streamline research. With the increasing importance of risk-sharing in the pharmaceutical industry to offset costs, CROs have begun offering a wider range of services, business arrangements and drug-hunting expertise to become true partners in drug development.

A common theme among the emerging and new alliance approaches is that more diverse players are engaged. These diverse partners are working together in innovative ways by fully leveraging talent and expertise, unlocking synergies on many levels and harnessing more brainpower across diverse players. One of the key aspects to these new approaches is a back-and-forth flow of information and trust. This is achieved by removing silos and facilitating an ongoing exchange of information, talent and expertise among each of the entities/stakeholders involved, resulting in more integrated relationships that are true partnerships.

We describe two distinct types of these non-traditional alliance models that integrate stakeholders as true partners and add value to the drug development process.

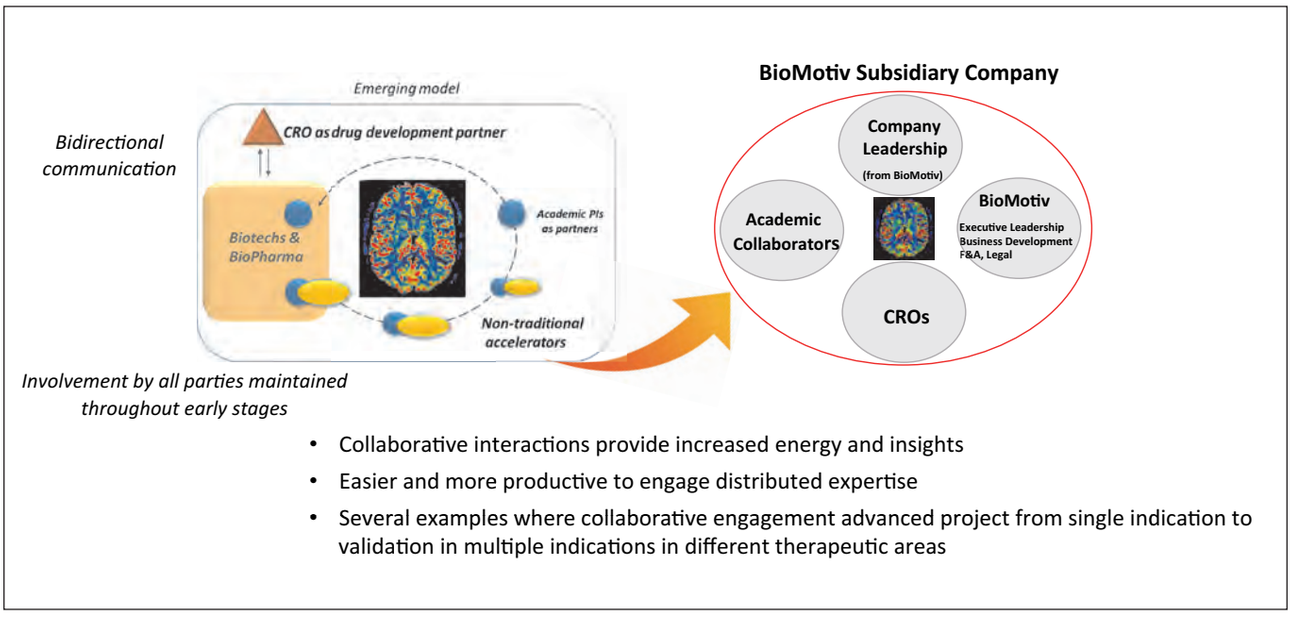


Figure 3: Non-traditional accelerators engage academic PIs and CROs in close interaction

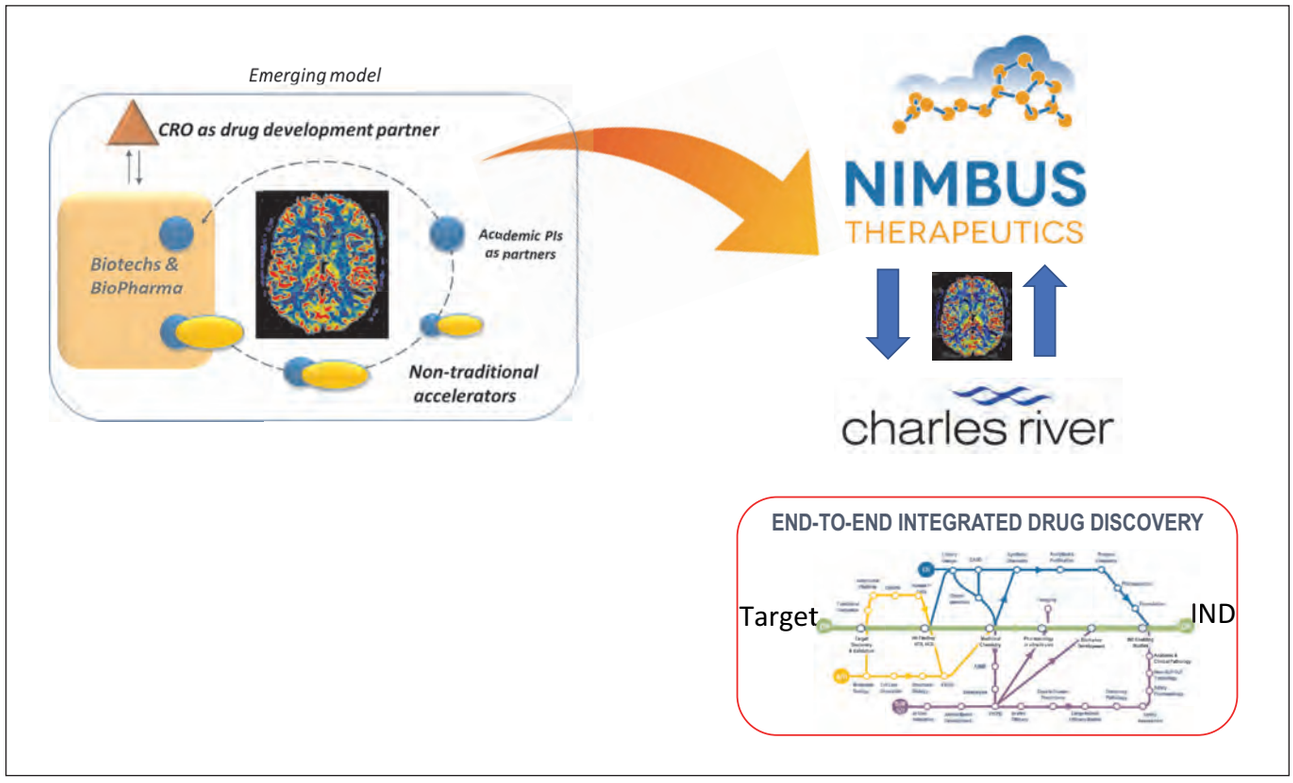


Figure 4
Biotech-CRO alliance for drug development testing emerging model using 1-Program experiment

The accelerator: engaging academic PIs and CROs in close interaction and leveraging distributed expertise

BioMotiv is a for-profit accelerator that is affiliated with The Harrington Project for Discovery and Development, a non-profit dedicated to supporting the creation of therapeutic breakthroughs based on the innovations of physician-scientists. BioMotiv addresses the limitations of traditional accelerators with an innovative model that provides a novel link between academic projects and late-stage commercialisation partners. While traditional accelerators do simplify the difficult and lengthy process of helping academic and scientific innovations become commercial products, most often these projects fail to make it to the next level. Typically, the tenure of resident start-ups is cut short due to the heavy burden on a small company to continue to raise funds, manage operations, forge partnerships and achieve the milestones needed to reach a value or partnering inflection point.

To support its partners through these trials, BioMotiv engages with PIs and very early-stage therapeutics companies well before they become attractive to larger biotechs, biopharmaceutical companies or venture capital firms. BioMotiv provides resources and hands-on guidance while working closely together with the PI or scientific founder to continue to flesh out understanding of the pathway and drug candidate, a key to garnering interest from biotechs and biopharmaceutical companies down the road. In this model, BioMotiv provides tactical and strategic leadership as well as business development support for the early-stage company and secures CRO involvement, with Charles River playing a major role as a drug discovery and development partner, and brings diverse drug development expertise and consultants to pivotal early-stage studies. This type of active collaboration greatly energises a project, offers insights into the development path for these early-stage companies and leverages distributed expertise effectively.

The biotech and the CRO: an alliance integrating sources of expertise to accelerate drug development

The biotech company Nimbus Therapeutics has developed extensive drug discovery and technology partnerships with leading industry, academic and government organisations. As part of Nimbus' unique outsourcing model to design and develop breakthrough medicines, its team also

works with many CROs on a fee-for-service or full-time equivalency basis. In early 2017, Nimbus and one of those CROs, Charles River, launched a multi-year strategic partnership to test an innovative new model for an alliance.

Nimbus and Charles River operate in an integrated, cross-company, fully-accountable team and work together to advance selected new programmes from discovery to investigational new drug submission (IND). In this model, Charles River contributes resources and collaborates closely during all phases of scientific effort to advance the programme, rather than following the more typical CRO fee-for-service model, where a CRO is paid for specific services or deliverables. As part of this unique alliance model, Charles River is eligible to receive potential milestone payments from Nimbus for certain undisclosed programme advancements.

An alliance like this is possible because Nimbus and Charles River have a long-standing successful track record of working together under the fee-for-service model, and Charles River has the diverse expertise and wide range of services to partner from discovery to IND. The hallmark of this model is the opportunity to combine the strengths of the two companies while preserving the diversity of their scientific perspectives. Additionally, because this is an alliance instead of a fee-for-service relationship, both companies share the risks and rewards. The operational benefits to Nimbus include time savings, reduced costs and a streamlined workflow from working with one CRO rather than engaging and managing dozens of different vendors. In addition, the arrangement gives Nimbus the opportunity to rapidly scale its operation and pipeline. Charles River benefits from the opportunity to develop further drug discovery and development expertise as it expands its business model to become a more integrated drug development organisation. It also gives the CRO the opportunity to make the best possible use of its significant and growing drug discovery expertise and pool of drug hunters. Patients can be expected to benefit as well from more efficient, faster and more cost-effective drug discovery and development.

Improving partner selection and optimising execution are fundamental keys to successful emerging alliance models

All successful development efforts require validating the science on which the effort is based. For emerging alliance models to be successful, not only must the science be strong but the members of the alliance must select the right partners and then mature their collaboration, ensuring that everyone on the project team is fully engaged and project-focused, and that incentives are aligned. The effort of scouting for the right alliance partners can be challenging; but being persistent, insistent and not settling for a suboptimal partner organisation is critical to success.

There is also an art to go with the science of building a successful alliance. Success requires getting ego out of the way and achieving compatibility among partners. This is essential for creating bi-directional and trusting relationships that tap into the full range of knowledge and skills in the alliance. It is also essential that all partners invest in the relationship during, before and after it is established, examining and re-examining procedures and processes (and simplifying overly complex internal systems), bolstering bi-directional communication channels and effectively managing expectations.

Innovative alliances can shift the drug discovery paradigm

Today, the costs of bringing new drugs to the market has risen, while the success rate for new drug development remains the same in the pharmaceutical industry. With this grim reality, what is the solution when both costs and expectations are at an all-time high? Many companies have found their solution to this problem by expanding their collaborative network and forming alliances. Through alliance and partnerships with other companies, academics, venture capitalists and other entities in the drug discovery ecosystem, the risk involved in drug development is spread out and diminished, while the reward for successful drug candidates can be shared to all players' satisfaction. With the cost of drug development so high, and with such a small margin of success, the benefits of risk-sharing and flexibility far outweigh the drawbacks of sharing credit with partners and stakeholders.

Innovative alliances can prove useful for eliminating inefficiency, responding quickly to breakthroughs, overcoming scientific, regulatory and business hurdles through co-operation and thereby expediting the delivery of therapy to patients. Innovative alliances can also bring together traditional players in new relationships that more fully leverage the strength and diversity of each organisation, and magnify the value for each company and the patients they hope to serve. It is a matter of rational as well as emotional consideration: the

drugs, and by extension the companies behind them, can further leverage working in true partnerships for the benefit of suffering patients. DDW

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