



Strategic Outsourcing in Early Clinical Development

Dominique Demolle and Denis Gossen of Aepodia explore the challenges and opportunities to achieve fundamental business model transformation

Pharmaceutical development is facing an urgent need for a fundamental transformation. Until now, most pharmaceutical industries have been using external providers of services on an ad hoc basis, essentially for capacity. But enriching the early drug pipeline requires radically different R&D approaches – for example, the externalisation of core expertise, functions and activities. It is not easy to outsource activities associated with translational medicine or ‘quick kill’. This should be defined proactively and with caution in order to generate a positive return on investment (ROI) in terms of speed, quality and cost. Significant transformation of the pharma business will require not just one but several models for developing new types of partnerships.

FROM ‘CAPACITY’ TO ‘CORE ACTIVITIES’ SOURCING STRATEGY

The last decade has been the theatre of significant changes in the pharmaceutical world. Mergers and acquisitions have become increasingly common, but they are not the only solution to either the innovation gap or the productivity equation. The model used by the pharmaceutical industry to develop drugs – conducting huge efficacy trials and launching products with tremendously expensive market force – is behind us. Various strategies to enlarge company portfolios via compound in-licensing, co-development or biotech acquisitions have pioneered different and more collaborative business models. Mirroring these changes, the outsourcing of some of the drug development activities to services providers has smoothly evolved into ‘strategic partnerships/collaborations’.

But this business model evolution is indeed a complex matrix leading to a significant and perhaps radical transformation: it is simultaneously about the ‘what’ and the ‘how’. Translational medicine, tailored therapies and personalised medicine are pathways to increase the probability of success and eventually provide faster, better treatments for patients, but these strategies must be linked to thorough improvements in development processes in order to reduce cycle time, as well as alleviate the increasing costs of developing new drugs (\$1.2 billion (1)).

Evidently, service providers/CROs must adapt to the situation, since they are facing the same business

transformation challenges as the pharmaceutical industry itself. This is of particular importance in early clinical development. Exploratory clinical development is still considered a core business area and is not largely outsourced, except on rare occasions. This is understandable in so far as the decision, taken at the end of the exploratory plan, seals the future of the compound and is the first step for the company as it makes significant drug development investments. But the situation is evolving: Eli Lilly has opened the door to ‘outsourcing’ early-phase development plans up to proof-of-concept (POC), first internally with Chorus (testing a radically different working model) (2), and secondly with strategic external vendors. Other companies have set up alliances for the implementation and management of their early phase activities, while keeping the ‘science’ based internally.

FROM TRADITIONAL SERVICE PROVIDERS TO ‘PARTNERS’

Despite different business model constraints, both the sponsor and the partner – that is the CRO – will agree jointly on developing a compound in a way that is as efficient as possible. In his new role, the partner is no longer only an ‘implementer’ of tasks decided and designed ‘in house’, but also becomes a *bone fide* ‘drug developer’.

Critically, the sponsor and partner(s) must agree on the type of approach that should be taken. Indeed, depending on the client portfolio, compound platforms and overall strategy,

the plan may vary from a ‘quick kill’ to a full, translational medicine approach. It is essential to define the common goal as early as possible, which should invariably address ‘the quality of the decision’ made at the end. In some respects, by agreeing to optimise the compound development, the partner(s) may contribute to discriminating between molecules, some of which may be stopped after early data generation. The fundamental difference between a ‘service provider’ and a genuine ‘partner’ lies in the fact that a partnership is a long-term alliance. In this paradigm, the partner becomes part of the mechanisms used by the sponsor to optimise the early clinical pipeline.

PATH TO 2020

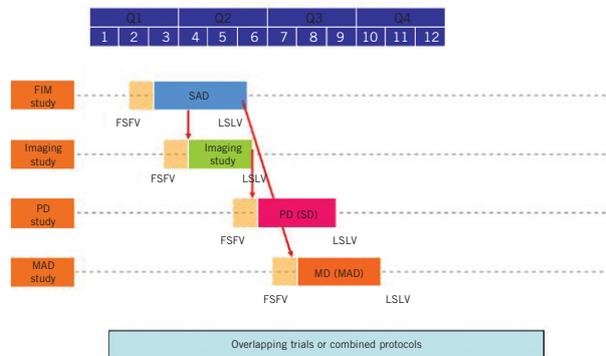
After the objectives and the strategic intent have been defined clearly, roles and responsibilities must be agreed upon between the parties before moving ahead with the development planning and implementation.

In the past, studies were conducted sequentially. But, nowadays, the model has evolved towards the use of ‘combined protocols’. This has contributed to cycle time reduction, albeit with some limitations. When all expertises are accessible in a single study site, combined or multiple-part protocols may be used; this is now routine and widely practiced across regions. This does not necessarily spare resources (especially upfront), as changes or new data may affect the full protocol, in turn introducing the risk of increasing timelines. Nevertheless, the overall gain is generally significant compared to a more traditional approach.

Increasingly, access to different types of patient populations, specific pharmacodynamic measurements and different kinds of expertise will require that an early phase clinical plan is conducted in more than one centre or country.

In this case, one has to revert back to using separate protocols: in order to reach POC with timelines comparable to combined studies, individual trials that trigger a decision point need to overlap with the preceding ones (see Figure 1). This is achievable provided that it is supported by solid regulatory know-how, as well as excellent operational planning and coordination. Past experience has shown that this is not easily achievable for a sponsor, mainly because of

Figure 1: Example of an ‘adaptive clinical plan’ where a combined protocol (or independent but overlapping trials) contribute to significant cycle time reduction compared to sequential studies with traditional timing requirement between trials (due to internal approval processes) – not shown in this figure. The separate but overlapping trials approach allows ‘geographical’ or ‘site’ independency when combined protocols require all the different expertises, access to population to be available at a single centre. (First in man (FIM); single dose administration (SAD); single dose (SD); pharmacodynamic (PD); multiple dose administration (MAD); multiple doses (MD); first subject first visit (FSFV); last subject last visit (LSLV).



the complexities of company approval processes (protocol review and approval, for example) – the weight of internal decision-making processes often slows down the overall plan. As an alternative, the pharma sponsor may then want to use a CRO as a ‘transforming agent’ to test and optimise procedures, with the view of possible future internal use.

The flexibility of moving to the next study (or study part) without final study data or reports requires strong and robust processes and SOPs. Important decisions are taken on these ‘interim data’. The quality standards are non negotiable: first of all, for the safety of the subjects/patients, but also because it will shape the future of the compound.

It can be anticipated that, by 2020, drug development will encompass several iterations of small efficacy and safety trials in targeted populations, where regulators might agree to dosing in specific populations, indications or number of patients as soon as data are generated (1). We need to be prepared for 2020 and consider that each of the studies presented in Figure 1 might potentially be a critical trial in the initial submission dossier or at future stages.

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KNOW-HOW AND AGILITY

Sponsors (pharma and biotech) now expect partners to also offer innovation, particularly when it comes to providing access to specialists or improving productivity by reducing cycle time.

From our experience, sponsors look for a combination of performance, expertise and excellence. This is creating significant changes in the type of workforce that is required. It is no longer sufficient for service providers to have junior employees trained for repetitive tasks. Instead it is important to be able to provide access to experienced staff members with a background in drug development and know-how in complementary disciplines, and who possess excellent leadership and communication skills.

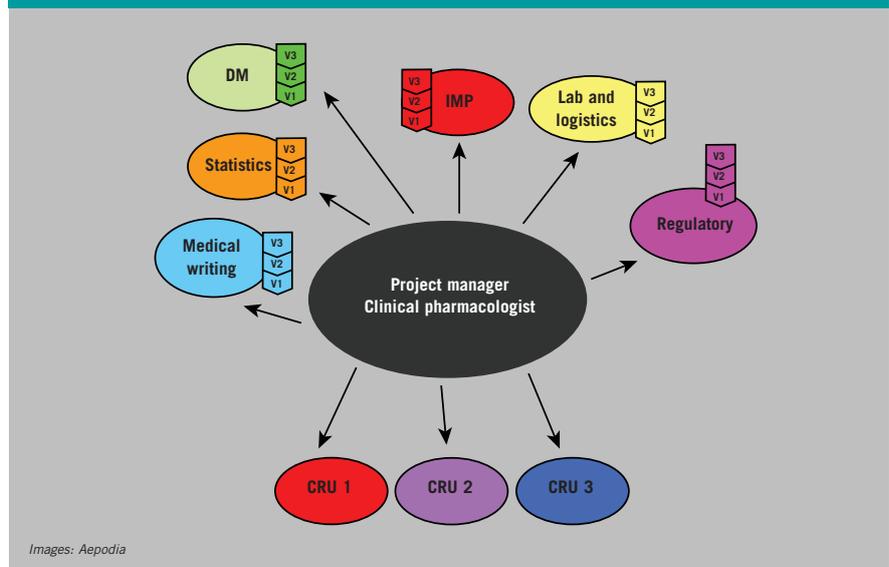
The sponsor must have absolute trust in the partner's ability to manage and deliver results. A strong risk management plan and agile management of projects and study related activities must be a core competency of the partner. In addition, and in a similar fashion to the Chorus model, the partner may give the pharma company an opportunity to test other ways of developing compounds without waiting for internal transformation to be fully implemented and operational.

INCREASED NETWORK

Another benefit for a sponsor in using a specialised partner in early clinical phase activities and compounds development is gaining indirect access to a myriad of experts and niche providers. It quickly becomes an exponentially growing network of experienced drug developers with early-phase drug development backgrounds, used on a 'fit for purpose' basis. One may argue that it is inefficient to re-create a team each time. There are, however, ways to optimise this, such as using standardisation, securing preferred vendors (as for data management) and project leaders experienced in early clinical development who will efficiently manage these experts and niche providers. Such an approach will maximise innovation. Figure 2 represents a typical example of the number of players in a given project. The ideal model for a given project is a balanced combination of preferred and niche provider-consultants.

Nowadays, CROs themselves may have outsourcing strategies: function aligned; central vendors (combining multiple supports); niche providers; or a mix of all three.

Figure 2: When the outsourcing strategy is function-based, a project manager may have to manage a large number of services providers (sometimes different vendors (V) per type of activities), as well as function representatives. This is only efficient if the roles and responsibilities are defined in great detail upfront. The key to success is a proactive and extensive definition of accountabilities and a highly skilled study coordinator/project manager.

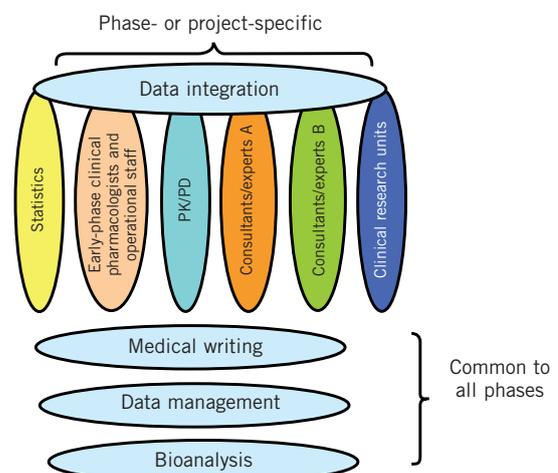


MULTIPLE MODELS FOR AN EFFICIENT STRATEGIC OUTSOURCING

Minimising risk while ensuring flexibility and innovation are contradictory concepts: strategic outsourcing is the ideal combination of different models. Sponsors are not the only ones to outsource anymore – they now delegate this responsibility to preferred vendors and pharmaceutical industries, akin to biotech.

From the 'volume' approach, which still makes sense in late clinical phases, we are evolving towards a 'specialist' approach in exploratory clinical development. The 'two to three preferred vendors' model, used in late phases, and support functions model are being replaced by a

Figure 3: The outsourcing strategy may be functionally aligned or phase aligned, or a combination of both; the real challenge is the ability to exchange, use, integrate and interpret data without silos from preclinical up to and including clinical, as an iterative process. The data flow must be planned proactively and is an integrated part of the overall project.



delegation of early clinical development activities to specialised scientists.

The fundamental transformation will be the sharing and integration of information from preclinical up to and including clinical activities independently from the sourcing model. The real challenge resides in the ability to exchange, use, integrate and interpret data without silos from the early discovery and across the development phases as an iterative process (see Figure 3).

Both ‘volume’ and ‘niche’ providers may co-exist, and indeed each of them fulfil a different business need and objective. Discerning pharmaceutical companies may choose this level of flexibility in order to maximise external focus, reduce cycle time and take advantage of innovations that others may bring.

Note

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About the authors



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