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Partnering is the secret to winning the Open Innovation Lottery

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“Open innovation - in a world of widely distributed knowledge, companies cannot afford to rely entirely on their own research, but should instead buy or license processes or inventions (i.e. patents) to other companies. Internal inventions not being used in a firm's business should be taken outside the company.”¹

Introduction

Between 2007 and 2009, 30% of all newly marketed medicines were either existing drugs or new formulations of old drugs². As a direct consequence of the success of this style of drug development, in 2012 the NIH National Centre for Advancing Translational Sciences announced their initiative for drug repurposing. In 2012, 58 compounds were made available for repurposing, with the intention that any new use will belong to the academic centre / commercial institution responsible for the idea. Assisting this process are a number of open source databases, grants, and open innovation industry teams.

Open innovation development is held to the same high standards as elsewhere in the drug pathway, and this presents a challenge for those directly responsible for the associated clinical trials, and to the life science company providing the compound. Compliance and oversight remain vital for such trials, and there is a danger of risk averse institutions dropping out of the drug repurposing initiative, with an associated loss to society.

Furthermore, the repurposing pathway will still require access to a number of highly specialised skills. Small to mid-size institutions must build effective pathways to access these skills, overcome the challenge of maintaining regulatory and safety compliance, and at the same time still derive maximum success from these opportunities.

We believe that effective partnering is essential, and this must be done in a collaborative manner, preferably with a single or limited number of partners to minimise ambiguity of responsibility. This paper draws on experience from a long-term Kinapse partnership, which has supported numerous drug repurposing trials.

1. Open Innovation: The new imperative for creating and profiting from technology, Henry Chesbrough, University of California
2. Graul, Al et al. Drug News Perspect. 2010 (PMID: 20155217); 2009 (PMID: 19209296); 2008 (PMID: 18301807).

Background to Open Innovation & Drug Repurposing Projects

Bringing a completely novel therapy to market is a well-known challenge

Lead times of 10-15 years and development costs of \$1.3 billion are par for the course. Despite this, pharmaceutical companies have enjoyed significant success – relying on a model that places multiple drugs into clinical trials, looking for the small handful that will reach the market and generate revenue. Those drugs that are successful generate enough revenue to fund the attrition within the rest of the portfolio – and it is this attrition has driven the growth in drug repurposing....

Drug repurposing is the application of an existing therapeutic molecule to a new disease indication, and at the core of this idea is the potential to deliver new therapies with shorter lead time, lower costs, and a greater potential for return on investment. Years of traditional drug development mean that for each success story, there are now staggering numbers of drugs with clinical data and/or pre-clinical. Furthermore, for each pre-clinical candidate, there are yet more molecules that were screened and rejected. The Drug Repurposing Hub³ holds a collection of 4,707 compounds with their associated literature-reported targets, and yet this is a fraction of the hundreds of thousands of molecules that have been subjected to some degree of investigation.

Several industry and Health Agency bodies are now championing the idea of open innovation

For example, making compounds available for repurposing by academic institutions, non-profits and start-ups. When seen through the lens of traditional program management constraints, the advantages of such initiatives are clear:

- Time: Many approved molecules with indications, have detailed information available on their pharmacology, formulation and potential toxicity. Because repurposing builds upon previous research and development efforts, new candidate therapies could be ready for clinical trials quickly, speeding their review by Health Agencies and, if approved, their integration into health care.
- Cost: There is evidence that drug repurposing can reduce the cost of bringing a drug to market by a factor of 101. This makes it an attractive proposition within product portfolios.
- Quality: Many drugs available for repurposing have already been marketed, and have already successfully passed through clinical trials. In many cases a repurposed drug will benefit from known safety & stability profiles – highlighted perfectly by the successful repurposing of the antiemetic thalidomide to treat multiple myeloma. Finally, repurposing has the potential to reduce off-label use, and the challenges inherent within this practise.

The merits of this approach have not gone unnoticed, and many Big Pharma companies now have business units specifically aimed at drug repurposing: AstraZeneca Open Innovation, Pfizer Indication Discovery Unit, Bayer Healthcare Common Mechanisms Research group, Novartis' New Indications Discovery Unit. These are now joined by a number of niche organisations, all of whom are contributing to the success in this field (Cures Within Reach, Cycle Pharma, Biovista).

3. The Drug Repurposing Hub: a next-generation drug library and information resource
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5568558/>

Why is Partnering so Important?

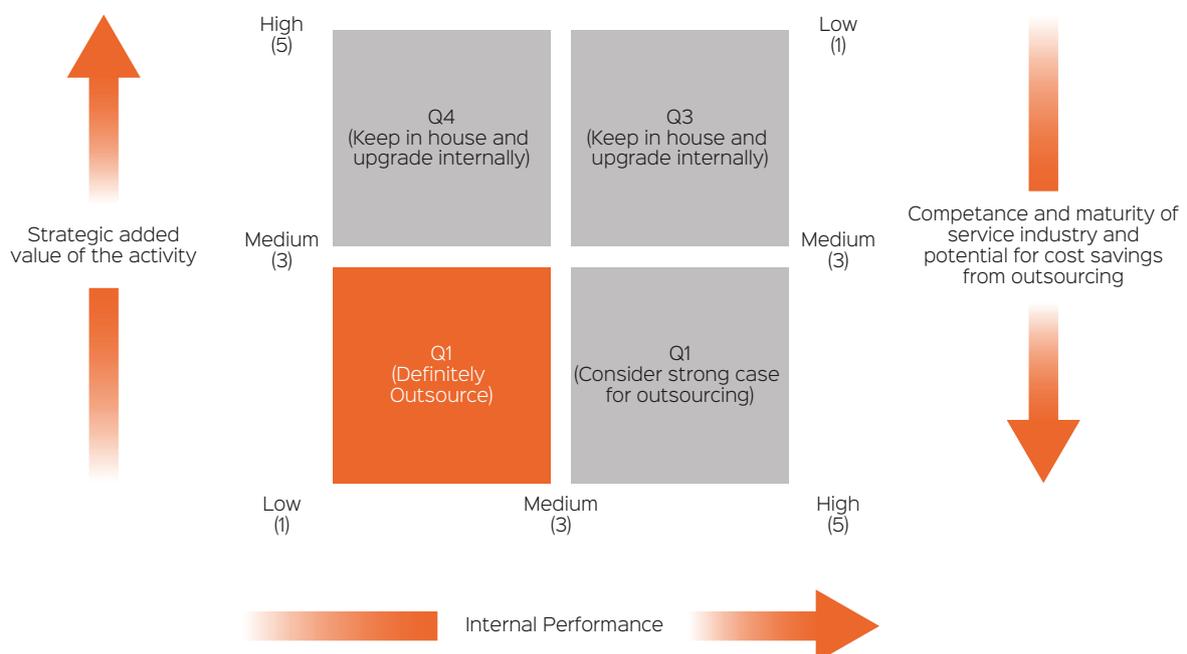
Access to expertise remains a fundamental challenge for many drug development institutions. A number of development activities are so specialised that it is unlikely that even mid-tier pharma companies will hold all the required skills. One such example is the recent requirement for lay person /plain language summaries – an emerging requirement, needing a vastly different skill-set from that found within traditional medical writing departments. Additionally, sponsors of drug repurposing programs often struggle to decide which aspects of development should be kept in-house vs. what should be outsourced, and within this decision there is further nuance regarding spreading activity across a number of vendors vs. partnering with a single provider.

In recent years, Kinapse has reviewed a number of client outsourcing strategies, working to marry company objectives to a robust selection criteria (see figure 1, below). Often this involves a fundamental shift away from a purely cost-driven approach. Indeed, two major concerns within the drug repurposing model go beyond the traditional parameters of time-cost-quality:

- **Safety:** whether the program be academically led, or the product of a small Biotech, there are likely to be skill gaps with respect to product safety.
- **Oversight:** The ICH R2 Addendum makes it clear that sponsors cannot simply contract out responsibility for clinical oversight. As the number of vendors on a development program increases, so does the oversight challenge. Furthermore, there is an expectation that signal detection operates across related products in a portfolio – potentially compounding this problem.

Kinapse has previously suggested the below framework to support outsourcing decisions. However, many institutions engaged in drug repurposing will not be in a position to consider in-house vs. outsourcing a capability. Instead, the discussion must be focussed on the manner of outsourcing across each service.

Figure 1: THE KINAPSE FRAMEWORK ASSESSES ACTIVITIES BASED ON 1) THE EXTENT TO WHICH AN ACTIVITY IS DEEMED AS A SOURCE OF STRATEGIC ADVANTAGE, 2) THE EXTENT TO WHICH OTHER COMPANIES IN THE SAME INDUSTRY OUT-SOURCE IT, 3) HOW WELL THE COMPANY PERFORMS THAT ACTIVITY, 4) THE DEGREE OF EXPERIENCE AND SKILL EXHIBITED BY THE SERVICE INDUSTRY IN PERFORMING THAT ACTIVITY, AND 5) THE POTENTIAL FOR SAVING COSTS BY OUTSOURCING



Drug repurposing institutions need sufficient self-awareness such that they know their weaknesses, married with enough development understanding that they can construct proposal requests and contracts that draw the appropriate level of support from a vendor – by doing so, they move away from a sponsor-vendor model, and are likely to realise the benefits of a partnership.

Tables 1 through 4 explore the advantages gained by partnering with a single vendor across all or a selection of services. Fundamentally, it is the ethos behind the word partnership that is often lacking when commercial engagements are discussed. Shared risk budgets, willingness to freely exchange process improvement ideas and technology solutions, and KPIs that measure both sponsor and vendor performance are all hallmarks of a mature partnership. Anything less is simply a contractual relationship and is unlikely to realise the efficiencies possible across interrelated services.

Table 1: Drug Safety Partnering

Outsourced Function	Key Advantages	Kinapse Recommendations
<p>Drug Safety Services</p>	<p>Economies of scale Outsource partners can work across multiple clients and pass on savings. Working at scale also allows individual clients to benefit from a partner’s collective experience.</p> <p>Scalable capacity Again, working at scale allows a partner to carry sufficient resource to meet demand peaks as needed.</p>	<p>A single partner for all drug safety requirements, contracted for 3-5 year term.</p> <p>Agree financial incentives that will drive innovation, and long-term quality of service.</p>

Drug safety represents a challenge for small biotech & specialty pharma, as often this role is delivered by a small team or single individual. In these circumstances it can be a challenge to build long-term institutional knowledge across a portfolio – especially if working with a small number of products across differing disease areas. Kinapse recommends that partner selection processes are designed to identify those vendors that promote from within, suffer low attrition, and can demonstrate processes for responsibly sharing appropriate safety updates across related programs. Doing this ensures that a carefully targeted budget can yield a service that delivers the same benefits as enjoyed by Big Pharma.

Table 2: Quality & Compliance Partnering

Outsourced Function	Key Advantages	Kinapse Recommendations
Quality & Compliance	<p>Access to niche expertise and capability that may not be required on a full-time basis.</p> <p>Access to innovative methodology which can enable step changes in business processes and free up resource for other value adding activities.</p>	<p>Consider adding this service alongside other partnered activities.</p> <p>Plan for routine partner support on day-to-day activities, so full time internal resources can focus on priority business objectives Use ad hoc SME input for new regulations and one-off situations.</p>

Early engagement with experienced quality & compliance professionals will deliver significant benefits to growing institutions. Being ‘outsourcing ready’ realises significant cost savings when attempting to externalise a function. Likewise, an experienced Q&C partner will understand the importance of building a scalable quality management system framework that reflects the need to maintain robust compliance with minimal training or maintenance-burden across development teams.

Table 3: Clinical Trial Disclosure Partnering

Outsourced Function	Key Advantages	Kinapse Recommendations
Clinical Trial Disclosure Services	<p>Access to niche expertise and capability that is unlikely to be required on a full-time basis.</p> <p>Access to innovative technology which can enables step changes in business processes and free up resource for other value adding activities.</p>	<p>Fully externalise this suite of services with a single provider to realise potential efficiencies.</p> <p>Plan for a long-term partnership, as over time, product familiarity will lead to further cost & time benefits.</p>

In an evolving area such as disclosure, the approach to contracting must be flex to support ad hoc access to expertise. Requests for proposals and subsequent contracts should be structured such that there is an expectation that the outsource partner will proactively highlight changes in regulations, or potential improvements to aligned functions that can support the disclosure process.

Table 4: Clinical Partnering

Outsourced Function	Key Advantages	Kinapse Recommendations
Clinical Trials	For small biotech and/or spin-out enterprises looking to repurpose, a CRO represents the only cost-effective route to market.	A single clinical partner, with a volume discount contractual obligation to hold down costs. Sharing product development plans can secure resources as part of a mature partnership.

Perhaps the greatest scope for success or disappointment sits with clinical outsourcing. Even within drug repurposing programs the clinical investment is likely to consume a significant chunk of the overall program budget. The challenge is to secure the best possible clinical service, whilst being just one trial to vendors possessing clients who are commissioning potentially hundreds of trials. In this situation, the currency of trust is extremely valuable. Agreeing to share development pipeline information, in return for repeat access to a trusted clinical team has advantages across the partnership. Likewise, agreeing terms for a risk budget, that can be accessed in specific circumstances represents innovative partnering that can minimise clinical overrun.

In Summary

The field of open innovation and drug repurposing presents distinct advantages, but is not without challenge. By forming strong partnerships with service providers, institutions can access skills and capability that would normally be only accessible by big pharma. Such partnerships also nod to the R2 addendum guidance, as partnering with the same vendor can realise a number benefits, including oversight compliance.

About Kinapse



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Kinapse, a Syneos Health™ company, is recognised as a leading advisory and operational services provider to the global Life Sciences industry. Founded by professionals from the biopharmaceutical sector, the company provides its services across the full R&D and commercialisation life-cycle, collaborating with its clients to improve the lives of patients, through a unique Advise – Build – Operate delivery model.

19 of the global top 25 Life Sciences companies rely on the breadth of Kinapse's world class advisory and operational services to analyse, implement and perform a wide range of projects and programs across global markets, delivering quantifiable business benefits and operational success.

Head-quartered in the UK, Kinapse has over 700 staff located in Europe, India and USA.

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