

# Kinapse



Life Sciences Consulting and Outsourcing

## **Kinapse White Paper**

## **Discovery Innovation – Productive Partnering For Shared Success**

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# Discovery Innovation – Productive Partnering For Shared Success



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Kinapse Consulting, 2010

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Partnering is an integral feature within today's pharmaceutical industry. While the conventional wisdom suggests that Phase II represents the optimum 'sweet spot' for big pharma product deals, our analysis reveals that discovery and early-stage clinical alliances are of increasing importance to big pharma's long-term business strategy.

This paper highlights the shifting industry trends responsible for the growth in earlier-stage partnering and describes how key stakeholders in the discovery space are evolving. We discuss the implications of this changing landscape for big pharma, and outline the new competences required to maximize value, mitigate risks and ultimately deliver new treatments to market.

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## **Big pharma are increasingly pursuing externally oriented discovery strategies in order to generate robust and diverse clinical development pipelines capable of delivering innovative new treatments**

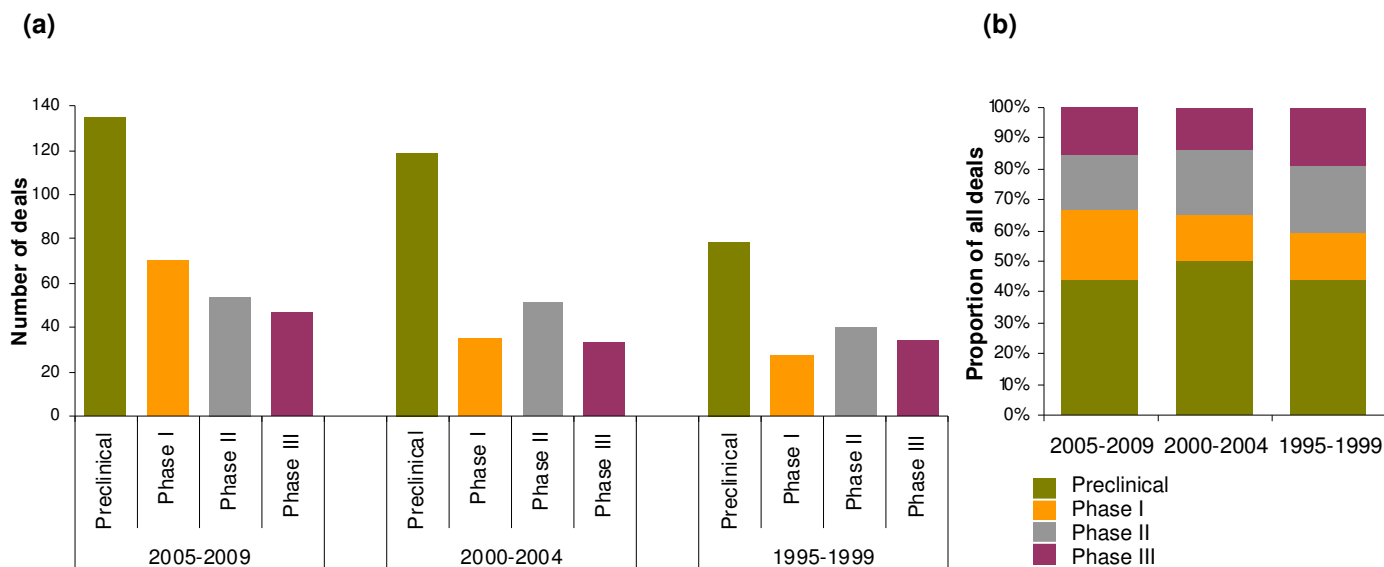
Partnering is an integral strategy within today's pharmaceutical industry, as big pharma seek to access innovative new compounds and best-in-class capabilities in order to ensure long term competitiveness.

In terms of new product development the biotechnology industry represents a rich source of novel therapies for big pharma, evidenced by the seemingly endless spate of high profile – and high value – pharma-biotech deals<sup>1</sup>. Our analysis shows that during the 5 year period 2005-2009 there were 306 reported licensing deals between biotech and top 20 pharma for R&D assets, compared with 238 during 2000-2004 and 180 during 1995-1999 (Figure 1), representing a period-on-period increase of around 30% in overall deal volumes. Notwithstanding the possibility of differential reporting between periods, this indicates that big pharma are increasingly adopting externally focused strategies to augment pipelines and expand portfolios.

Because of the inherent uncertainty and risk associated with drug development, transactions

designed to fulfil short and medium term strategic requirements typically involve relatively well characterised assets such as marketed products and late stage development projects. Accordingly, conventional wisdom points to Phase II as the 'sweet spot' for pharma-biotech product transactions<sup>2</sup> – i.e. typically after demonstration of clinical proof of concept but before the commitment to large scale Phase III studies. There is clear competence based rationale for Phase II partnering, with biotech providing specialist and proprietary technology expertise and a culture conducive to product innovation, whilst pharma brings capabilities in large scale clinical development and sales & marketing. Furthermore, the Phase II partnering model aligns with the prevailing capital structure of each sector. Achieving clinical proof of concept creates a point of inflection that represents a significant decrease in R&D risk and a corresponding increase in project value. By developing assets to this stage, high growth biotech companies can therefore generate substantial value for their own shareholders while simultaneously creating a risk profile more attractive to big pharma and its investors.

Despite the conventional wisdom, our analysis also indicates that big pharma are increasingly pursuing earlier stage deals (Figure 1). Although the proportion of preclinical deals has remained relatively constant for each 5 year period –



**Figure 1 | Big Pharma deals by development stage:** a) Number of deals reported between biotech and top 20 Pharma companies during the 5 year periods 1995-1999, 2000-2004 and 2005-2009; b) Proportion of deals for assets at each stage of development during the 5 year periods.

Source: Kinapse<sup>3</sup>

accounting for around half of all deals – there has been a significant shift towards earlier stage partnering for clinical assets. During 1995-1999 and 2000-2004 around 22% of Pharma-biotech deals were for Phase II assets, while Phase I deals accounted for only 15%. More recently this position has reversed; the number of Phase I deals doubled from 35 during 2000-2004 to 70 during 2005-2009, constituting 23% of all deals for the latter period, whereas the number of Phase II deals increased only marginally from 51 to 54 – representing 18% of all 2005-2009 deals.

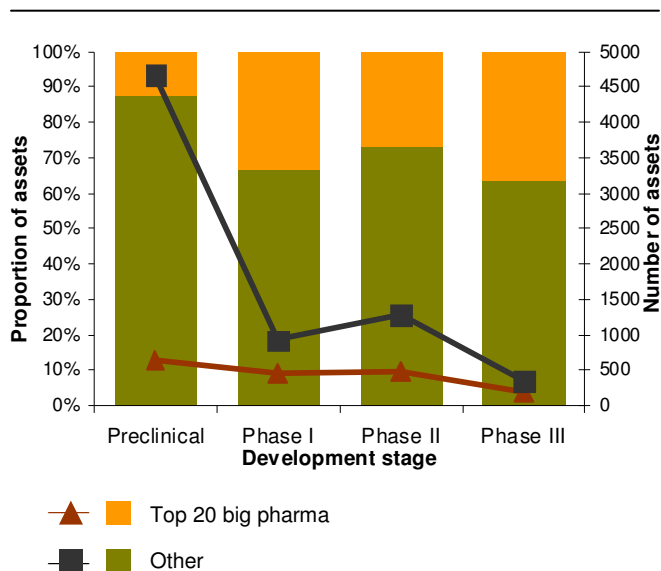
While the growth in early stage deals is likely to reflect increasing competition for later stage assets, this trend may also signify more fundamental shifts in the forces influencing R&D supply and demand. On the supply side, biotech companies with innovative early stage assets but insufficient funding are more readily positioning themselves as discovery partners and/or acquisition targets for big Pharma. Meanwhile new discovery organisations emerging from academic, government and charity sectors are playing progressively more significant roles in the

translation of biomedical research into promising therapeutic candidates, and represent a growing source of innovative potential therapies for big Pharma. On the demand side, big Pharma appear to have decided that broader, more diverse portfolios are required to deliver sustainable revenue growth in the much vaunted post-blockbuster era of personalised medicine, and are increasingly externalising discovery activities by engaging a range of different parties in order to identify, secure and realise value from innovative compounds and technologies (Table 1).

Faced with a relative abundance of promising early stage therapeutic opportunities (according to the Pharmaprojects database, 88% of active preclinical assets currently reside outside of big Pharma pipelines, compared with 64-73% of clinical stage assets (Figure 2)), big Pharma must develop core competences in early stage partnering and alliance management in order to maximise value, mitigate risks and ultimately deliver the promise of innovative new treatments to patients.

**Table 1| Recent examples of big pharma discovery externalisation**

<b>Deal structure</b>	<b>Partners</b>	<b>Details</b>
Big pharma/ biotech alliance	Roche/ Synta	<p>In January 2009 the partners announced a strategic alliance to discover, develop and commercialise small molecules targeting a novel family of ion channels with a role in rheumatoid arthritis and other inflammatory diseases. Roche will fund research conducted by Synta during an initial two year research period, and receive worldwide rights to certain products identified prior to the end of the research period. Synta retains certain co-development and co-promotion rights. Roche will pay all preclinical, clinical, and commercial costs.</p> <p>Synta will receive \$25 million in upfront cash license fees and committed research support, of which \$9 million will be provided in the form of research support over the initial research period. Synta will also be eligible to receive development milestone payments of up to \$490 million for three licensed products across multiple indications, and commercialisation milestones of up to \$170 million for each of the three products. Synta will also receive tiered royalty payments on any future product sales.</p>
Big pharma/ academia research collaboration	AstraZeneca/ Cancer Research Technology	<p>In January 2010 the partners announced an innovative jointly-funded 3 year multi-project R&amp;D alliance to discover and develop novel small molecules targeting cancer metabolism.</p> <p>AstraZeneca will take the most promising projects forward into pre-clinical and clinical drug development - through an innovative model for sharing the risks and potential rewards in creating new anti-cancer treatments. CRT will receive milestone payments and royalties on the projects that AstraZeneca take into clinical development.</p>
Joint venture	Merck & Co./ Wellcome Trust	<p>In September 2009 Merck and the Wellcome Trust announced a pioneering joint venture with a not-for-profit mission to research and develop affordable vaccines for low income countries. The partners announced that they would contribute equally to an initial investment of £90 million (c. \$143 million) over the first 7 years and share decision making rights in new entity – The Hilleman Laboratories – which will be based in India and support around 60 researchers from 2010.</p> <p>The R&amp;D joint venture will operate with a combination of core funding from the founders, third party grants, and other revenue streams. Over time, it is envisaged that the entity will enter into partnerships with numerous public and private organisations, each of whom will have the option to retain commercial rights to products developed by Hilleman Laboratories, provided affordable and broad access to low income countries is secured.</p>
Corporate venture investment	Novartis/ Ascent	<p>In December 2008 Ascent and Novartis Option Fund entered into a license option agreement, which provides Novartis with rights to co-develop drug candidates against a specific GPCR target. The agreement includes an upfront fee, potential milestones totalling &gt;\$200 million and product royalties.</p> <p>Novartis Option Fund also participated in Ascent's Series A, which raised \$19 million in October 2007.</p>
Restructuring discovery units	GSK Discovery Performance Units	<p>In July 2008 GSK announced the creation of small Discovery Performance Units (DPUs) within its existing Centers of Excellence in Drug Discovery structures. Based around the view that discovery is best optimised through research by small, focused teams, each DPU comprises between five and 80 researchers and focuses on a specific biological pathway.</p> <p>35 DPUs have been funded on a 3 year business cycle from a new global Drug Discovery Investment Board, which is also mandated to ensure that future investment is allocated to competing DPUs based upon objective performance and value creation metrics. The Investment Board board comprises senior GSK R&amp;D executives, plus external individuals from the VC and biotech sectors. According to GSK CEO, Andrew Witty, the intention is "to drive a more ruthless, well informed and objective approach to capital allocation decisions in discovery."</p>
Corporate venture spin-out	GSK/ Tempero	<p>In May 2009 GSK established Tempero as a discrete inflammatory and autoimmune disease focused entity, in an extension of GSK's Discovery Performance Unit model.</p> <p>As a fully external unit, Tempero is positioned to seek VC investment in subsequent funding rounds. Further details are yet to be disclosed, however GSK are likely to have options to acquire rights to Tempero's assets at a predetermined value at future development milestones.</p>
Network hub	Sanofi-Aventis	<p>In May 2009 Sanofi-Aventis announced plans to convert its Vitry-sur-Seine factory near Paris to a biotech R&amp;D hub, with the stated intent of forging partnerships with other biotech and research companies.</p> <p>The Eur200 million (c. \$265 million) hub will be dedicated to research, development and production of biotech products and will create Sanofi-Aventis' first cell culture platform capable of producing monoclonal antibodies by 2012.</p>
Open innovation cluster	GSK/ Wellcome Trust/ UK Government	<p>In October 2009 GSK announced a partnership with the Wellcome Trust and the UK government to create a biotech science park on the site of its UK R&amp;D facility in Stevenage.</p> <p>Altogether the partners will invest £38 million (c. \$60 million) in cash and facilities to establish the cluster, which will offer companies shared access to specialist skills, equipment and expertise to stimulate new innovation in drug development. The cluster is anticipated to offer space for around 1500 scientists.</p>



**Figure 2| Active preclinical and clinical development stage assets owned by or under exclusive licence to big pharma:** The line charts represent the number of assets at each development stage and the stacked bar charts represent the proportion of assets within top 20 pharma pipelines.

Source: Pharmaprojects

### Discovery alliances require new partnering models

By partnering early, big pharma can better guide development and commercial strategies to ensure the greatest chance of success. Nonetheless, discovery assets represent high risk opportunities from a development perspective. Furthermore, the diverse range of potential discovery partners and associated stakeholders presents distinct challenges for early stage business development and alliance management in terms of how best to identify, access and develop the most promising early stage opportunities.

Managing the activities of disparate research groups in response to partnerships, alliances, M&A activity or internal restructuring requires effective organisational design and implementation. In recent years big pharma have adopted many different organisational frameworks designed to enhance the efficiency, productivity and effectiveness of R&D, moving

away from the traditional fully vertically integrated models towards horizontally and vertically disintegrated structures with varying degrees of success<sup>4</sup>. Whilst there are numerous different approaches to managing discovery alliances, in all cases organisations must implement the appropriate structures, processes and tools in order to effectively integrate internal and external discovery activities. Based upon an analysis of selected recent high profile big pharma discovery partnerships and our experience of supporting implementation of big pharma integrations, we have identified a series of critical success factors for big pharma discovery externalisation.

#### *Selecting the right opportunities*

Big pharma must possess the capability to identify and rigorously evaluate promising opportunities. Opportunity identification within big pharma should not be a reactive exercise reliant upon invitations from potential partners. Instead it requires pharma to engage in proactive environmental scanning and to create and exploit discovery networks that extend into academic, government, charity and SME sectors. Opportunities must be evaluated objectively according to a robust scorecard that incorporates technical, commercial and financial criteria and highlights the associated risks. Crucially, evaluation of early stage opportunities requires a clear appreciation of long term strategic objectives, and therefore it is imperative that the process of opportunity evaluation involves decision makers from all relevant functions.

#### *Creative and flexible dealmaking*

In order to access innovative discovery opportunities big pharma must re-evaluate traditional partnering strategies and move towards deal structures that reflect both the earlier stage nature of discovery deals and the more diverse range of stakeholder interests associated with the growing number of not-for-profit discovery organisations. Discovery partnerships are typically long term relationships in which partners expect to work together for mutual gain, and where success relies upon the continued commitment of each partner. Therefore it is important that transactions are structured equitably and provide the requisite incentives to all partners involved. Whilst traditional

components such as upfront, milestone and royalty payments are likely to continue to feature in discovery deals as means of apportioning value, big pharma should expect a growing emphasis on investment in collaborative and risk sharing infrastructure such as R&D funding, equity investments, non-commercial freedom-to-operate licences and technology transfer, that better reflect the strategic objectives of public and private research entities with early stage assets.

It is important to recognise that incongruent strategic objectives are not necessarily mutually exclusive, and therefore big pharma must develop a willingness to explore R&D strategies that fulfil the objectives of multiple parties. For example, discovery opportunities arising from charities and foundations often carry conditions that oblige commercial partners to develop for specific disease areas or particular geographical territories. Whilst such markets may not be strategic priorities for big pharma, they may represent acceptable opportunity costs in cases where assets also have clear potential to be developed for strategic markets. Moreover, in many cases securing initial approval or reimbursement in niche markets can markedly increase the likelihood of achieving successful subsequent applications in larger, more commercially important markets.

It is also important to recognise that alliances with not-for-profit discovery organisations are unlikely to offer big pharma the potential for future M&A opportunities that have become a common feature of commercially oriented alliances. Many successful licensing deals between big pharma and smaller commercial organisations eventually result in the acquisition of the smaller party. This allows big pharma to assume full strategic control of the asset and removes the uncertainty associated with an ongoing royalty obligation, whilst providing the shareholders of the acquired party with an opportunity to realise a return on their investment. However because of fundamentally different strategic objectives, not-for-profit discovery organisations do not generally represent feasible future acquisition targets for big pharma. Without the insurance afforded by a future acquisition opportunity, big pharma must use greater foresight in dealmaking and develop

more creative deal structures that incorporate a range of flexible options that provide for an array of different product and market scenarios.

#### *Fostering innovation*

To ensure the greatest likelihood of successfully developing an in-licensed or acquired discovery asset, the key drivers of innovation and success must be harnessed within the big pharma R&D engine. Drivers of innovation typically include (but are clearly not limited to):

- i) *specialist technology expertise* – many biotech companies are formed around a core proprietary technology platform or product opportunity and therefore possess deep technology and/or disease area expertise. Moreover, many such companies are founded by leading academics with active research interests that relate directly to the core technology.
- ii) *high project specific commitment* – in the product based model, the value of a biotech SME is typically inextricably linked to the value of its lead compound(s). Since compound value increases disproportionately as development risk is mitigated, companies recognise that greatest value gains can be achieved by focusing resources towards advancing a limited number (typically one or two) of leading compounds, as opposed to developing a larger portfolio to a less well advanced stage. As a result the fortunes of high growth biotech companies are often tied to the success – or otherwise – of their leading assets, thereby creating a high degree of commitment to individual projects.
- iii) *entrepreneurial approach to decision making and resource allocation* – in order to achieve the greatest returns on investment, biotech companies typically invest only minimally in capital expenditure, preferring to access capabilities on an as needed basis in response to prevailing demand. This demand based approach allows capabilities to be scaled according to available opportunities, permitting more efficient and effective resource utilisation.

To retain the drivers of innovation, big pharma must view originators not just as external sources of intellectual property but also as external sources of technology specific competences and capabilities that can be leveraged to ensure that maximum value is extracted from available resources. For example, utilisation of originators' deep disease area expertise is particularly important in the development of complex biological products where specialist knowledge of specific molecular and biological mechanisms of action is required. Expertise in disease biology is also important in small molecule drug discovery, with widespread use of techniques such as molecular profiling and biomarker development necessitating an in depth understanding of the basic biology underpinning compounds' mechanisms of action. Therefore big pharma should ensure that R&D strategies for partnered discovery assets utilise the full extent of originators' technology specific and disease area knowledge and capabilities in order to design innovative studies that demonstrate efficacy and value.

To derive full value from discovery partnerships all parties must embrace the full scope of shared commitments pertaining to ensuing relationships. Effective management of R&D partnerships requires investment in dedicated infrastructure to support collaborative working and information sharing. Whilst this invariably necessitates dedicated process and project management, big pharma must avoid introducing too much inflexibility so as to encumber innovation. To ensure success, big pharma must seamlessly incorporate alliance management capabilities into discovery project and portfolio management. For example, joint management bodies comprising representatives of all partners should be established for partnered discovery assets, and empowered with responsibility and accountability for project advancement. At the same time, in order to ensure parity with internal projects, all externally originating projects should be reviewed alongside internal projects as part of big pharma's periodic portfolio evaluation and prioritisation process undertaken at executive management level. Only by devising and executing partnering strategies that are simultaneously equitable, mutually beneficial and fully aligned with internal

portfolio decision making, will big pharma ensure the greatest likelihood of successfully bringing partnered discovery assets to market.

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