

License or Buy?

**Current Trends in the Biotech Sector and Recommended
Strategic Options:**

The UK Perspective

June 2008

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Recommended Strategic Options:
the UK Perspective**

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June 2008



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the UK Perspective**

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Non-confidential abstract

Pharmaceutical companies (pharmas) are desperate to solve their productivity crisis by sourcing new products and technologies from biotechnology companies (biotechs) to expand their existing pipeline. Observation suggests that there is an increasing incidence of big pharmas to making early stage biotech licensing deals and their pressing need might have translated to an increase in licensing cost.

At the same time, venture capitalist (VC) investors in biotechs are also driving earlier exits through trade sales in order to rationalize their portfolio and to dispose of any unattractive holdings, in contrast to taking the company to initial public offering (IPO) at a more mature stage. Recent trends show that the number of trade sales in the UK remains high and there is no sign of decline. Due to the inherent high risk profile of early stage biotechs, resulting valuation of these small entities are often much lower.

One proposition is that the pharmas might now ascribe a higher net present value for the licensing deal than the value being attributed to the entire biotech entity. However, the decision process in choosing the most desirable partnering option is a multi-dimensional problem and possible downsides have yet to be taken into account before drawing more definite conclusions.

This study first aims to provide a general overview of the current alliance activities in the UK biotech sector and to reassess how the current economic downturn might have impacted on recent trends. Furthermore, it offers comparative evaluation between the acquisition costs incurred otherwise for a few of the recent prominent licensing examples, and to reveal the various value drivers and inhibitors that have influenced the decision process. The final deliverables of this study are to provide the most suitable strategic recommendations to both pharmas and biotechs respectively.

Preface

I confirm that the material in this dissertation is not copied from any published work or material, unless it is clearly identified as such and a full source reference given.

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Signed

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Executive Summary

Last year (2007) was the first year that the number of mergers and acquisition (M&A) deals involving UK biotech companies (biotechs) superceded the number of licensing deals. A hypothesis for this change in trend is that the value of the licensing deals has increased to a point where the net present value of these deals is valued higher than the value attributed to the targeted biotech by the acquirers. Besides, desperation from the VC members of the board of the biotech requiring an exit might further impede the growth of value within these high potential biotechs. Under the current economic downturn and volatility in equity market, valuation of the UK biotechs may be suppressed to a point where to acquire could be a better financial option for the pharmaceutical companies (pharmas) than to license.

However, this assumption only compares the financial aspects between licensing and M&A whereas in reality, the problem involves much higher level considerations. Firstly, the acquirer's inherent attitude to risks in licensing is completely different from that in M&A. Acquisition involves a much larger upfront investment than licensing and the acquirers have to bear all uncertainties about the future development of the targeted biotech. On the other hand, licensing allows risk mitigation through tranche milestone payments and eliminates the need to integrate any liabilities attached to the acquired entity.

There has been more focus on achieving capital efficiency in biotechs and licensing is seen as an important source of non-dilutive financing. VCs experience higher pressure to exit as they get nearer to the end of their fund cycle, but their return on investment is highly dependent on the market status. Knowing that the UK IPO market is not optimistic, VCs have adopted a stronger stance on the trade-sale exit route for their portfolio companies.

For pharmas, the most effective partnering strategy differs on a firm-specific level and the decision is also strongly influenced by the prevailing market condition. It is preferable to acquire when the targeted biotech has more than one validated asset and the remaining entity can strategically dovetail into the pharma's business model. Appropriate post-acquisition integration is necessary to maximize the core value attained through M&A. Nonetheless, M&A activities are likely to increase in the UK biotech sector because there is an apparent need for some level of rationalization and consolidation.

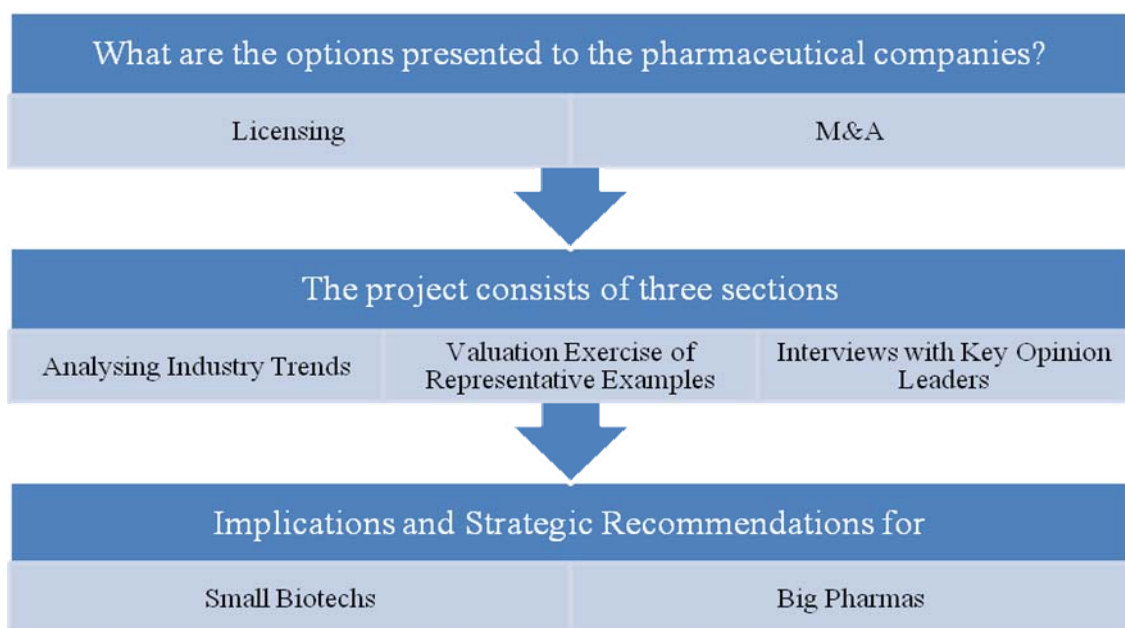
Chapter 1: Outline

1.1 Purpose of Study

A significant part of this study is to document both the licensing and mergers and acquisition (M&A) activities in the UK biotech sector in recent years. Based on the trends identified, the second objective is to find out the particular drivers and inhibitors that have led to observed changes. Further discussions on the general market dynamics are presented and relevant strategic recommendations are made based on the improved understanding of the UK biotech sector.

1.2 Structure and Approach of the Project

Initial data gathering involved extensive desk based research, followed by interview sessions with participants representing key industry sectors in the UK. As most of the existing knowledge and opinions surrounding this subject are applicable at a broader global scale, this study is tailored to gather data and yield conclusions specifically for UK based companies.



Chapter 2: Introduction

2.1 Defining the Scope of the Study

2.1.1 Types of Alliance in the Biotech Sector and Scope of the Study

Alliance is a generic term that is used to describe a family of partnering relationships, each distinguished by the degree of collaboration involved (see **Figure 1**). These relationships are strategic in nature between two (or sometimes more) interdependent parties, both motivated by the intention to harness the best benefits out of the partnering process.

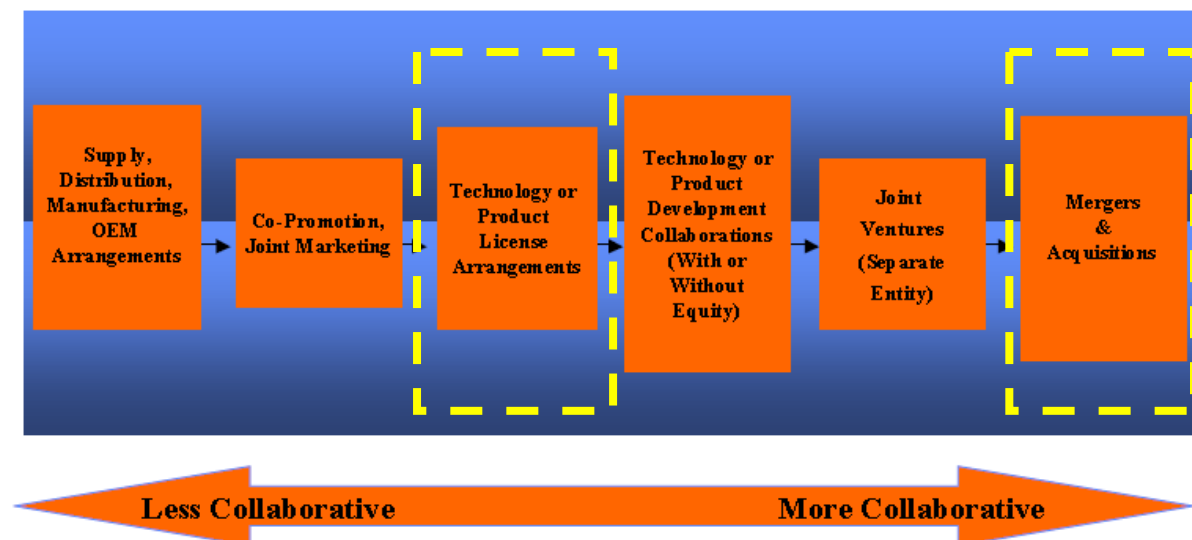


Figure 1 Common types of partnering relationships (Gleason, 2005)

Amongst the spectrum of partnering relationships, the scope of this study is restricted to strategic alliance options of licensing and merger and acquisitions (M&A) (as highlighted in yellow boxes in **Figure 1**). The critical component that connects these two partnering options is the common interest in innovative therapeutic products of both biotech companies (biotechs) and pharmaceutical companies (pharmas). Small biotechs rely on their ability to deliver new products in order to create value proposition. As for pharmaceutical companies, they can effectively fill their drying product pipelines through in-licensing valuable innovative assets from the biotechs, or to integrate the entire entity in-house through M&A.

2.1.2 Licensing versus Merger & Acquisition

Licensing

Licensing represents a simple, short-term transactional relationship between the licensor¹ and the licensee² where control over the asset being licensed is restricted to terms stipulated in an agreement and with limited time and scope (Boston Consulting Group, 2005). In particular, licensing between pharmaceutical and biotechnology companies is an agreement relating to the ownership of intellectual property (IP) rights pertaining to a technology, development compound or marketed product (Seget, 2006).

In the context of biotech-pharma alliance, “development collaboration” is a term that is often misused and confused with “licensing”. The underlying driver behind these two alliance arrangements is very similar, which is to gain access to intellectual property rights with regards to a certain asset. The main distinction is that licensing involves a simple transaction with some sort of continuing relationship between the licensor and licensee, but it may not imply any financial input from the licensor. For example, the licensor may still have development obligations that are funded by the licensee. On the other hand, development collaboration involves a significant continuing relationship between the companies in the form of co-development³ or co-commercialisation⁴ agreement (Seget, 2006).

¹ Licensor: the person who gives the license

² Licensee: the person who receives the license

³ Co-development implies funding is coming from both parties

⁴ Co-commercialisation is a comprehensive agreement that includes co-promotion and co-marketing between the two parties

Drawing up licensing agreements is a complex process which involves setting the basis on the rights to be licensed, the exact nature of the license, how royalties are payable, and the conditions of termination (Ranade, 2008). The cumulative value of a licensing deal is influenced by the type of partner, merit of innovation, stage of development, scope, and type of agreement (Arnold et al, 2002). Other more subjective factors, such as the quality of managers and scientists, also play important roles in determining the total perceived value of the licensing deal.

Typical payments in a licensing deal are dissected into the following categories:

- i) Upfront payments:** payments made at the time when agreement is secured
 - a) Cash upfront; and/ or
 - b) Equity: occasionally equity investments are made whereby the licensee would acquire an undertaking to secure partial rights to the licensor's assets
- ii) Milestone payments:** payments based on successes at various stages of development
 - a) Development milestones: event milestones such as commencement of subsequent phase of clinical trial or acceptance by a regulatory body.
 - b) Sales milestones: payments is usually triggered when aggregated sales exceed a certain pre-negotiated amount
- iii) Royalties:** payments are made based on percentage of sales after commercial launch. Such percentage can be a fixed percentage, or it can be an escalating royalty percentage depending on sales performance.

Mergers and Acquisition (M&A)

In M&A, the acquirer expends resources to gain complete control through ownership of assets and capabilities of the acquired company. Although most of the M&A deals are exclusively acquisitions, they are still termed M&A. The legal status of the old entities change and the acquirer would then assume full responsibilities for any risks those acquired assets incur (Boston Consulting Group, 2005). M&A investment also bears uncertainties about the future development of the acquired firm.

For public companies, the value of an M&A transaction is the sum of the trading value of the targeted firm and the acquisition premium. An acquisition premium is the difference between the actual cost of acquisition and the estimate of the targeted firm's value by the acquirer before the acquisition on a stand-alone basis (Financial Definition, 2008). Such premium is partly based on precedent transactions in the sector, and it also correlates to the synergy benefits realised by the acquirer.

For private companies that do not have a trading value, the value of an M&A transaction can be justified according to the increased value above the precedent funding round. The value of the company does not only lie in its lead pipeline product, other value drivers also play a critical role in a biotech's valuation, such as potential cost synergies and radical enhancements to existing operations (Ranade, 2008).

2.2 Drivers for Alliance

2.2.1 Big Pharma

A pharmaceutical company is defined as a vertically integrated organisation, which engages into value-adding operational chain spanning from research and development (R&D) to distribution (Hopewell, 2003). Although the so called ‘big pharmas’ are the old giants in the pharmaceutical industry, it is unlikely that they will be able to survive on their own research and pipelines as “the science is too big, broad and extensive for pharma to do it alone” (Howard, 2004). The bigger issue is that they have become so big in revenue terms that they can no longer generate enough new in-house products to replace their current revenues when current products come off patent.

The most repeatedly referred-to problems in the pharmaceutical industry are firm-specific capability constraints and universal industry threats. By and large, the R&D productivity of the pharmaceutical industry is currently sub-optimal (Cole, 2004) where pipeline output is low and declining. In order to maintain a balanced portfolio, pharmas are actively searching for new products to achieve alignment within their intended strategic development across therapy areas, geographies and time-scales. The threat of excess human and physical capacities relative to the returns that could generate has also been a potent driver towards alliance on a more firm-specific level.

One of the major universal threats in the pharmaceutical industry is mounting regulatory hurdles, which is exacerbated by the problem of revenue constraints. In 2007, only 16 small molecule drugs and 2 biologics gained FDA approval, which was a record low number since 1983 (Dion, 2008). Drug development legislation in the UK was also tightened after the infamous clinical trial failure with TeGenero’s TGN-1412. Pharmas continually have to reassess their business strategies due to the heightened safety scrutiny, which increases the difficulty in getting approvals for novel drugs. Moreover, radically increased healthcare costs have driven consumers and regulators across the major drug markets to control costs, which would hinder revenue generation of the pharmaceutical industry.

At the same time, pharmas are faced with the loss of blockbuster patents; it is estimated that drugs with about US\$20bn worth of annual sales will face patent expiry in 2008 (BL Research Bureau, 2007). Upcoming fierce competitions of generics represent a massive loss of revenue which will not be easy to replace. As these drugs are coming off patent, Datamonitor estimated that 40% of 2005 brand sales worth about US\$157bn, will be cannibalised by generic competition by 2015 (Belsey et al, 2006).

2.2.2 Small Biotech

Small biotechs can be characterised by the inherent differences in their business model and their field of research with respect to a pharmaceutical company (Hopewell, 2003). Core biotechnology companies are the ones that actively engage in early stages of the drug development process, or are involved in developing enabling technologies that would enhance the drug discovery operations. Apart from the rare few successful exceptions, most biotechs in Europe remain as relatively small or medium sized businesses with less than 50 employees. These are mainly research focussed entities, with the aim to provide intermediate products or knowledge (through licenses and patents) for the pharmaceutical industry (Kranich, 2008), and most often with inadequate sales or marketing capabilities.

The major challenge for small biotechs is to stay in business long enough to develop and commercialise products (Class, 2003). The average cost of developing a new biotechnology product is estimated at \$1.2billion (The Tufts CSDD, 2006), which reflects the costs of drugs that fail in testing and the time costs from inception to market. Lengthy clinical development process takes on average 97.7 months to complete. In addition, full launching of the product to obtain reimbursements in all the major markets takes another two to three years, and peak sales are only anticipated five years post-launch. On top of difficulty in raising sufficient finance to support high cash-burning activities, other inherent problems of biotechs include sub-critical R&D capabilities, high infrastructure costs and inefficiencies, poor business models and management.

Besides raising funds through public or private sources, establishing strategic alliances are particularly crucial for a young, resource-constrained biotech start-up. Alliances enable the firm to gain access to diverse information and capabilities with minimum costs of redundancy, conflict and complexity (Baum et al , 2000). In addition, a firm's strategic alliance can also influence other's perceptions of its capabilities by providing access to external legitimacy and status (Stuart et al, 1999).

2.3 Factors that can Influence the Decision upon M&A as Opposed to Licensing

2.3.1 Distinction between M&A and Licensing

When faced with the problems described above, pharma are eager to bring biotech's capabilities in-house. Piecemeal approach through a series of licensing deals is a popular option. Alternatively, acquisition of small biotechs that can be easily integrated can improve performance and increase shareholder value (Burrill & Corp, 2007) because it is an effective solution to bridge the short- to mid-term revenue gap by gaining access to

- 1) IP technology, products, revenue stream, sales outlets/ distribution network;
- 2) Manufacturing facilities and expertise and
- 4) To increase value of acquired entity/ product (Arnold et al, 1999).

As for the small biotechs, being acquired enhances the likelihood that the assets of the biotechs can be fully financed. However for those who aspire to become a fully integrated pharmaceutical company, licensing is an effective way for the partners to combine complementary assets and to venture new business opportunities. Refer to **Figure 2** for further breakdowns for the differences in the inherent nature of the two alliance options as seen by the acquirer/ licensee.

As seen by the acquirer/ licensee		
	M&A	Licensing
Control	High Full ownership Unambiguous corporate governance	Low Flexibility and quick implementation One or multiple partners Benefits from network effects
Resources	“Hard” and therefore easy to value High redundancy High potential for economies of scale	“Soft” and therefore difficult to value Low redundancy Low potential for cost cutting
Regulations	No barriers to consolidation	Desirable in situations where M&A is impossible for legal or regulatory reasons

Figure 2 M&A and alliances differ on several dimensions, adapted and modified from BCG analysis (Boston Consulting Group, 2005)

2.3.2 Global Economic Downturn Impacts on the UK Biotech Sector

The general negative sentiment in the UK biotech public sector has dissuaded investors' interest in financing the notoriously volatile and unpredictable industry. Recent reports have raised concern upon the on-going poor performance of the UK biotech public market. An analyst at Seymour Pierce (Davoudi, 2008) concluded that 2007 had been a “disaster for biotechnology in the UK”. The credit crunch has further amplified the cyclical downward trend in the biotech sector, as shown in FTSE Techmark Mediscience Index⁵ dropping to levels last seen in 2004 (**Figure 3**). KBC Peel Hunt believed that such fall was a consequence of the extensive risk aversion in the biotech sector, with funds being removed to other growth sectors.

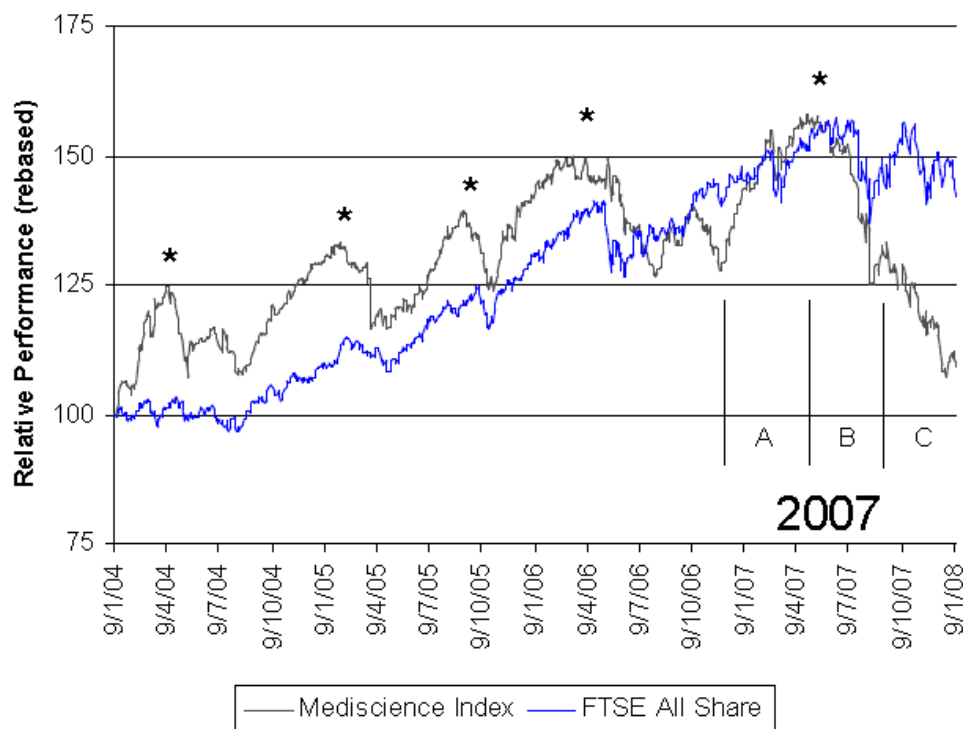


Figure 3 Relative performance of Techmark Mediscience Index to FTSE all share, adapted from (KBC Peel Hunt, 2008)

⁵ FTSE techMARK mediscience is a real-time index comprised of companies on techMARK mediscience market. Companies are those in Pharmaceuticals, Biotechnology, Medical Equipment and Supplies sectors, as classified by the FTSE Global Classification System.

Over-promising UK biotechs have failed to deliver value to shareholders and are worryingly in need of additional cash injection. An analyst at investment bank Cannacord Adams (Russel, 2008) showed that amongst the 66 listed biotech companies, only a mere 10 made a profit in their last reported accounts. Amongst the remaining 56 loss-making companies, less than half have more than 12 months of cash left to fund their research program. Therefore, market volatility has been an imperative that has forced small biotechs to look for alternative sources of financing or inevitably in some cases, these biotechs may have to be put up for sale or wound-up.

Funding gap persists

VCs are losing interest particularly in funding early-stage companies as they do not see a sufficiently profitable return to justify the associated high risk of their investments. With the declining amount of funds available in the European biotech sector (**Figure 4**), the outlook of the UK biotech sector is further diminished by prominent venture firms such as 3i (Arnold, 2008) and Merlin (Lewis, 2008) pulling out from funding early-stage start-ups. Small biotechs that are in the process of moving into downstream development suffer the most because they are at a critical phase of development. Insufficient financial support at the proof-of-concept clinical studies has challenged the small biotechs businesses to remain sustainable with high rate of cash-burning incurred in their daily operations (Ernst & Young, 2007).

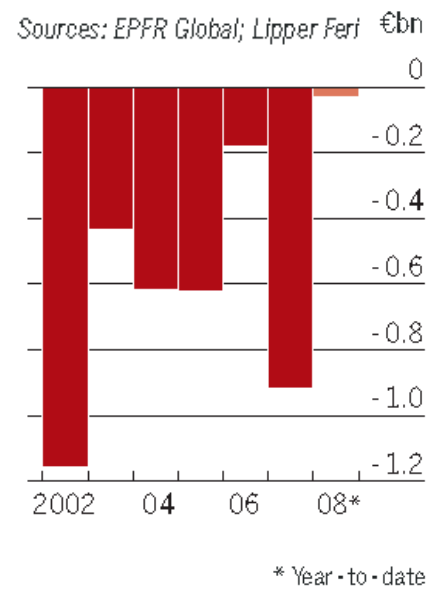


Figure 4
European biotechnology fund flows (Johnson, 2008)

Poor IPO environment

The number of UK biotechs pursuing an initial public offering (IPO) on the London Stock Exchange (LSE) has been decreasing over the past 3 years (**Figure 5**)⁶ and to date there has been no biotech IPO issued in 2008.

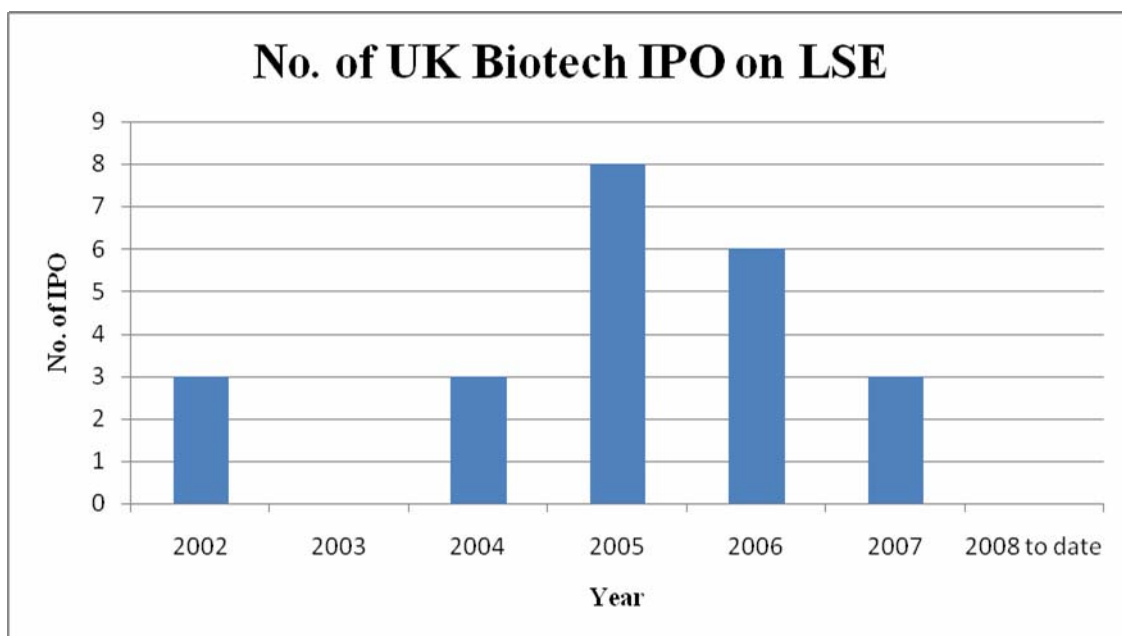


Figure 5 Annual number of UK biotechs IPO admissions on UK main market and AIM

With the current economic downturn, it is especially difficult to raise public funding for UK biotechs. The acute funding problem in the UK biotech market has meant that most listed companies are small and very few of them have the competence to reach successful commercialisation of a product in the full view of public investors (Johnson, 2008). In addition, the aspiration to generate long-term revenue streams from a blockbuster drug is offset by the high development risks. Therefore, today the IPO exit probably no longer exists as an option for the private investors in these small biotechs. They are holding higher hopes on getting a profitable exit through acquisition by a larger rival rather than allowing the market to establish what their investments are worth.

⁶ Graph is compiled from published data of LSE's New Admissions Summary of UK based companies. Imposed criteria for the short-listed companies include IPO-only, UK-based and those within the biotechnology subsector.

2.4 Motives and Deliverables of this Study

An observed behaviour in the industry is that pharmas are eager to foster closer relationship with biotechs and hence have boosted licensing activities aimed at the biotech sector. Established pharmas are mostly cash-equipped and hence can support the high cash burn-rate associated with most biotechs. With the relevant internal expertise to evaluate the technical and commercial potential of the opportunities arising as a result of these licensing alliances, big pharmas can gain access to promising candidates and boost their technological capabilities under favourable terms. Besides, desperation from the VCs on the board of the biotechs wanting to exit might impede the growth of enterprise value within these high potential companies. Under further influence from current economic downturn, valuation of the UK biotechs might have been suppressed to a point where the attributed value no longer directly corresponds to the actual asset value.

One of the propositions is that the pharmas might now appreciate a higher net present value for the licensing deal than the value being attributed to the entire biotech entity. This assumption might also link to pharma's potential inclination towards acquisition rather than to license the technology/ product of interest alone. However, the decision process in choosing the most desirable partnering option is a multi-dimensional problem. Possible downsides (such as resources required to integrate liabilities attached to the acquired entity) and upsides (such as revenue gained through the sale of non-core assets) have yet to be taken into account before drawing more definite conclusions.

Therefore, this study first aims to provide a general overview into the current alliance activities in the UK biotech sector and to reassess how the current economic downturn might have impacted on recent trends. Furthermore, it offers comparative evaluation of the acquisition cost that would have incurred otherwise for a few of the recent prominent licensing examples, and to reveal the various value drivers and inhibitors that would influence the decision process to pursue acquisition. The final deliverables of this study is to provide the most suitable strategic recommendations to both big pharmas and small biotechs respectively.

Chapter 3: Identifying Current Trends in the UK Biotech Sector

3.1 Methodology: Desk Based Research

In order to identify the trends in the UK biotech sector, an extensive search was done in various news databases⁷ over the period for the last five years for licensing deals in which a UK biotech company was an out-licensor, and for M&A deals in which a UK biotech was the targeted company. For the context of this study, the inclusion criterion for a UK biotech is defined as follows:

- i) A company with its head office located within the UK
- ii) A company with little or no revenue, but that is heavily investing in development pipeline products (biologics or small molecule drugs or diagnostics), or in the process of developing a platform that is capable of supporting such functions.
- iii) In most cases, the considerable proportion of value within the company comprises of one or more pre-clinical or clinical stage products. It may possess a marketed product with modest sales potential or is generating a small royalty interest. (Bennett S., 2004)
- iv) By and large, the revenues generated are not able to cover the R&D expenditures and the company remains net cash burning.

A database was compiled for these licensing and M&A deals respectively (refer to **Appendix 1** for the comprehensive list of licensing deals and **Appendix 2** for M&A deals). All known information of the respective deals used within this study was extracted from the public domain and therefore there are limitations in particular regarding the level of detail in cases where no specific information was announced.

⁷ Database used include the following: APM Health Europe, BioSpace, Biopharm Insights, Cambridge Healthcare and Biotech company database, Fierce Biotech, InfoPharm, News Analyzer

The trend analysis was prepared with the best available data and averaged financial values were calculated inclusively amongst the deals with at least two out of the three parameters (bio-value, upfront, milestones) present.

3.2 Identifying Trends, Findings and Analysis

The following section outlines the various aspects of key findings on changes in alliance trends, along with a short discussion to explain such changes with the previously acknowledged factors. Figures 6-13 are novel graphs plotted with raw data as shown in Appendices 1 and 2. These trend findings facilitated the drafting of appropriate interview questions, where interviewees were asked to comment on the data being presented.

General increase in alliance activities in the UK biotech sector

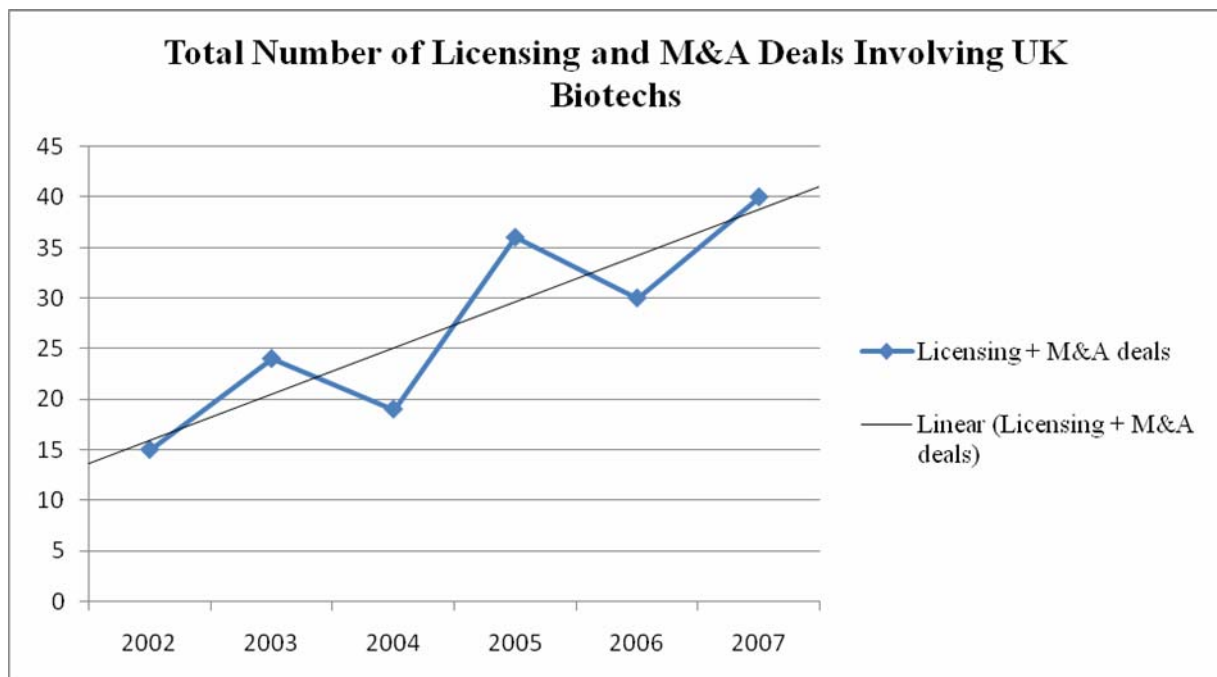


Figure 6 Total number of licensing and M&A deals involving UK biotech in years

Over the years, the UK biotech sector has seen a general increase in alliance activities, which is the consequence of a combination of push and pull incentives from the big pharmas and small biotechs respectively. In order to enhance shareholder value, big pharmas are required to demonstrate consistent improvements in earnings in the short term, and a longer term strategic position that gives shareholders the assurance that results will continue to meet the double-digit growth target.

As a result, big pharmas are aggressively branching into biotech to search for new opportunities and to maximise future opportunities in new therapeutic areas. In addition, biologics business is not vulnerable to generic competition due to the high degree of molecular complexity, hence pharmas can profit from much longer life cycle for than that from small molecules (Smith, 2007). Hence, it is seen as vital for traditional pharmaceutical companies to tap into the fast-growing biologics business in order to maintain their long-term competitiveness within the highly dynamic industry.

As for small biotechs, access to funding to sustain the cash-burning R&D growth for the company's unproven and high risk technology is perceived as the biggest challenge. This is particularly true for early-stage start-ups as they rely to a great extent upon VC funding. VC demands significant returns within a fixed timeframe, and the typical growth strategy would either be to develop the company with the intention to enhance its acquisition prospects, or to nurture a greater enterprise value through independent operations which ultimately leads onto IPO (Hamilton, 2005).

M&A activity has outpaced licensing activity

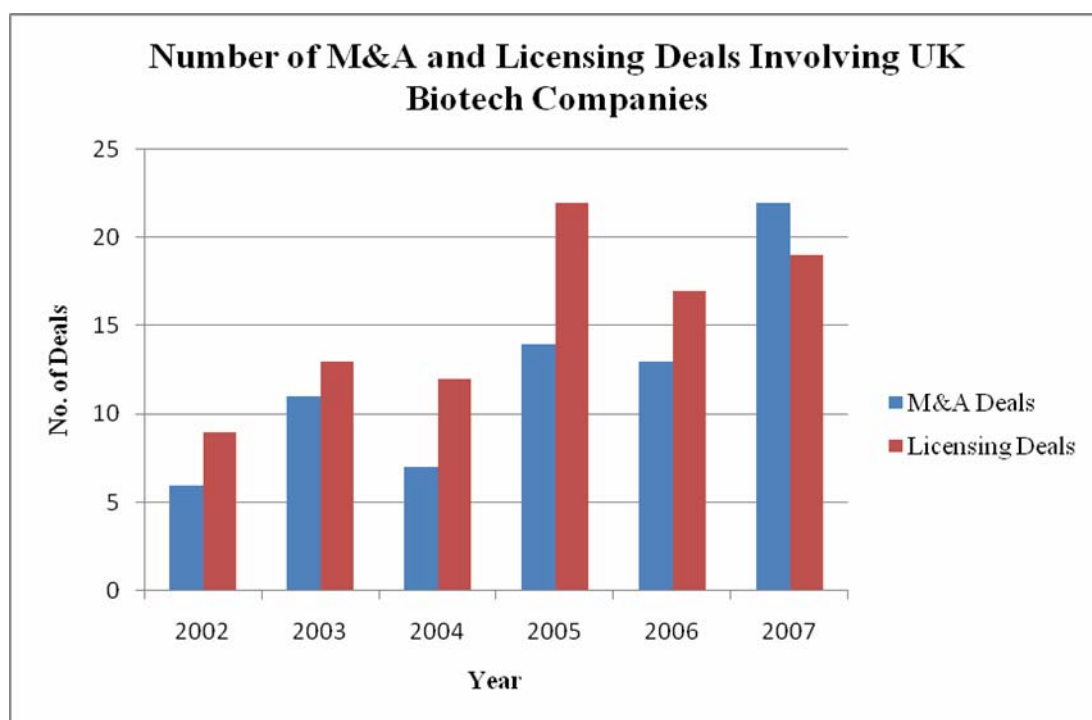


Figure 7 Number of M&A and licensing deals involving UK biotech companies, where UK biotech acted as the targeted company or the licensor

There has been a gradual rise in M&A activities within the UK biotech sector and interestingly, 2007 was the first year where the number of M&A deals superceded the number of licensing deals. An explanation for such a change in the view of a pharma is that acquisition of biotechs with substantial technology capabilities would be the most straightforward strategy to make a big leap to a stage comparable to other early pharma-biotech adopters. AstraZeneca for example, had missed out on the biotech opportunities during the initial biotech boom. It had since acquired several biotechs to expand its biologics pipeline and capabilities⁸. Further insights upon this matter would be discussed in Chapter 5 with new perspectives from various interview participants.

⁸ AstraZeneca had acquired Kudos Pharmaceuticals, Cambridge Antibody Technology and Arrow Therapeutics.

3.2.1 Licensing Trends

Number of out-licensing deal of UK biotechs and averaged 'bio-value' are rising

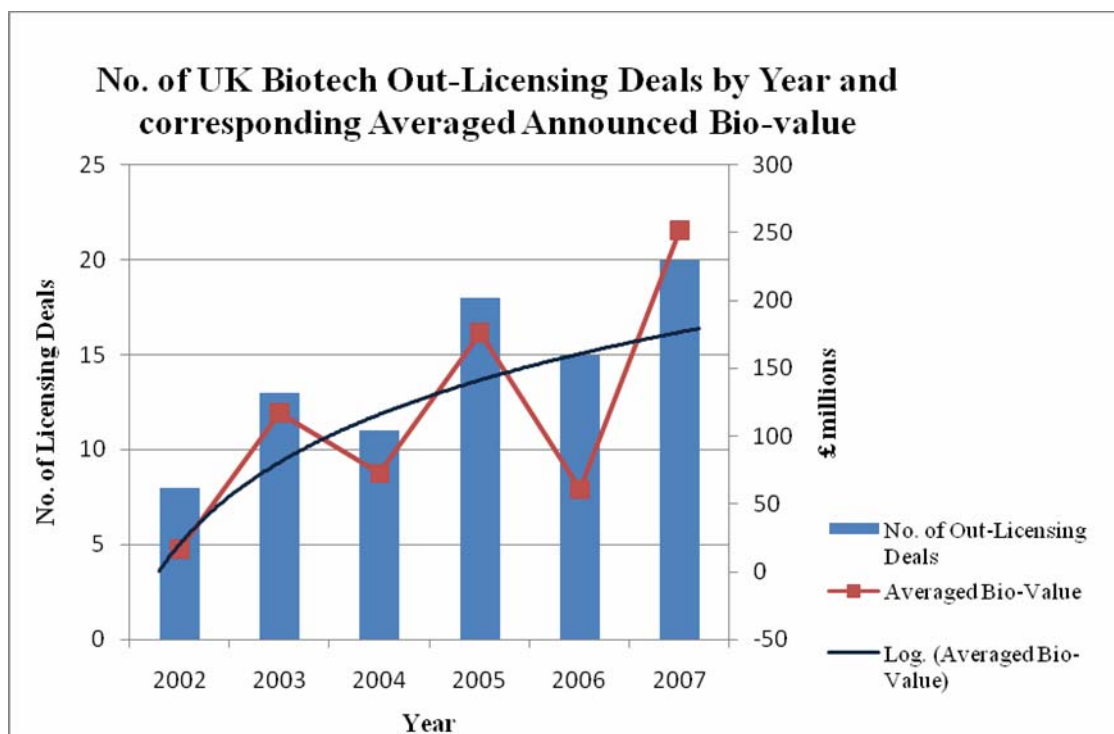


Figure 8 Number of UK biotech out-licensing deals and corresponding averaged announced bio-value by year

The bio-value is the announced value of the licensing deal, including the upfront, milestone and sometimes royalty payments. Over the past 5 years, there have been general increases in both the number of out-licensing deals carried out by UK biotechs and the corresponding bio-values⁹. The increase in the total number could be interpreted as pharma's desperation to implement short-term strategy to improve productivity by in-licensing products to fill gaps in pipelines (Seget, 2006). The increase in the deal value can be related to the relative increase in size of the deal to include multiple development compounds that incorporate further options to license other products developed in parallel.

⁹ The value for average bio-value 2004 and 2006 are skewed because the data pools in both years were small. The majority of the bio-value and details of the out-licensing deals remain unannounced and so it is likely that the rise would have been a better fit to the linear trend line.

Tendency towards back-end loaded licensing deals

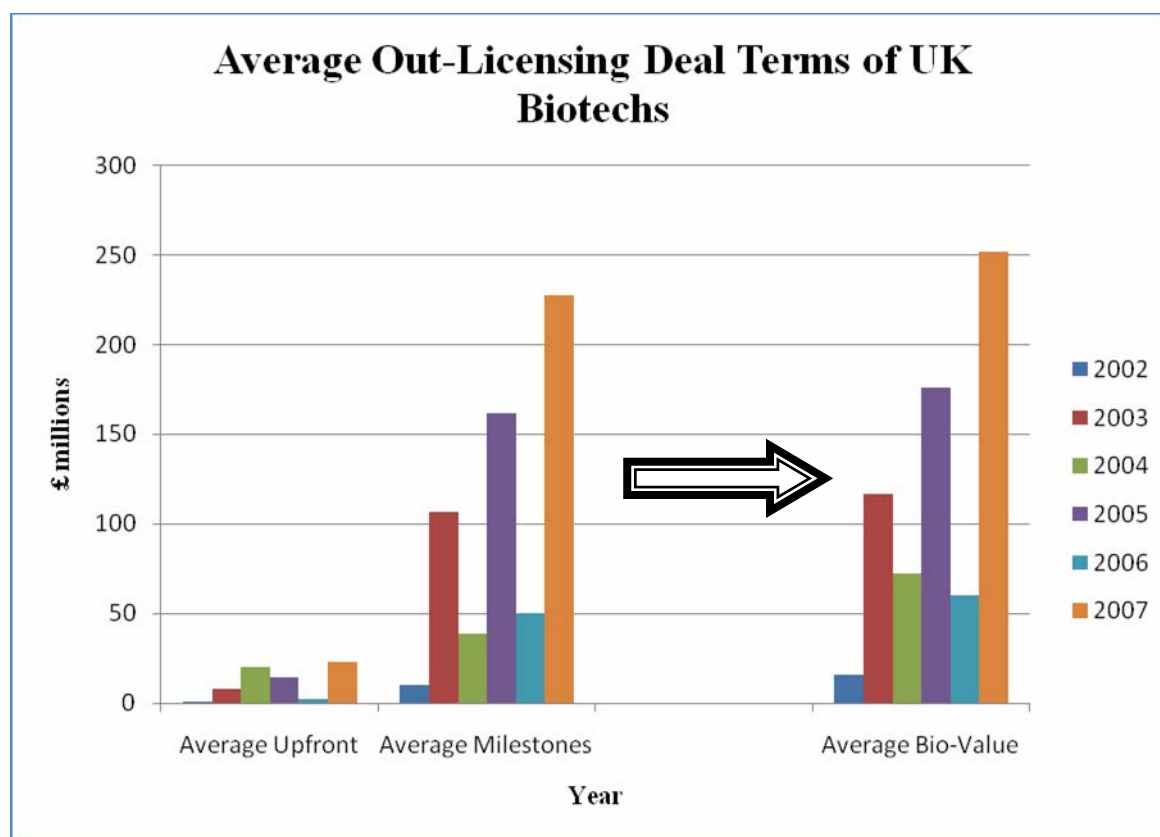


Figure 9 A breakdown of the average out-licensing deal terms of UK biotechs; there has been an increasing trend for average milestones and bio-value, but the values for 2004 and 2006 are skewed because of insufficient public data available.

In negotiating licensing deal terms, big pharmas would aim to back-end load the deal terms as much as possible to mitigate development risk that may be encountered. This means that the upfront commitments made are minimal in comparison to the amount payable for event milestones, and the pharma would not have to bear the full cost if the in-licensed product did fail. As shown in **Figure 9**, the average bio-value had increased and much of this increase was due to the rise in average milestone payments. There had not been a significant change in the average upfront payments and this observation could be part of the prevailing licensing strategies in the UK biotech sector.

Number of mid-stage out-licensing deals has risen

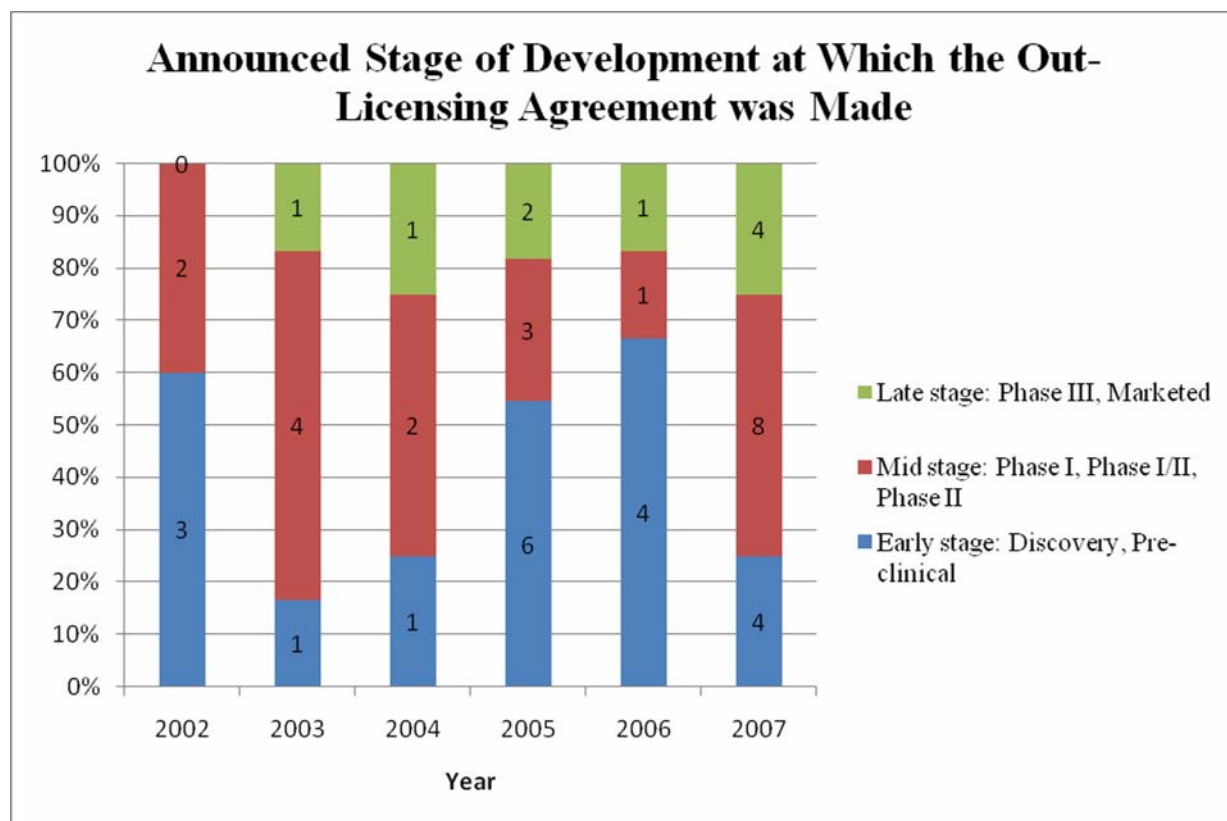


Figure 10 Announced stage of development at which the out-licensing agreement was made where a UK biotech was the licensor

There had been an increasingly larger proportion of early-stage out-licensing deals executed between 2003 and 2006¹⁰. In the past, the high risk inherent in early-stage products and the associated difficulty in assessing the market potential for these products had deterred big pharma's interests. However, with the UK biotech sector remaining relatively young, there were a limited number of companies with products in preclinical or clinical development that could be out-licensed. This effect of scarcity was exacerbated by the increasing number of licensing deals being performed over the years, where lucrative late-stage licensing opportunities were pretty much being picked over. The desperation from the pharma to get their hands on these promising products had created such a huge demand that could not be satisfied and consequently, pharma were forced to look further upstream at earlier stage innovations.

¹⁰ The proportion only took into account the stage of development being announced and so the total number of licensing deals does not correspond to the number addressed in earlier sections.

The amount of money put aside for pharma in-licensing was spread over a significantly larger proportion of early-stage development with inherent high risk profiles, but substantially lower in-licensing cost and much lower royalty rates. Therefore, such a pipeline would encompass a larger funnel of product candidates in order to allow for the high attrition along the development path (Ernst & Young, 2007), which further drove the increase in the number of licensing deals.

On the other hand, there was a sudden expansion into mid-stage out-licensing deals during 2007, with 6 out of the 8 being in phase II development. A product that has advanced further in the clinical development can command high value because the attrition rate is significantly reduced. Such a trend is consistent with the maturing of the UK biotech sector with emerging companies that have sufficient resources and capabilities to bear the risk of development.

Platform technology is no longer the “hot” area in out-licensing

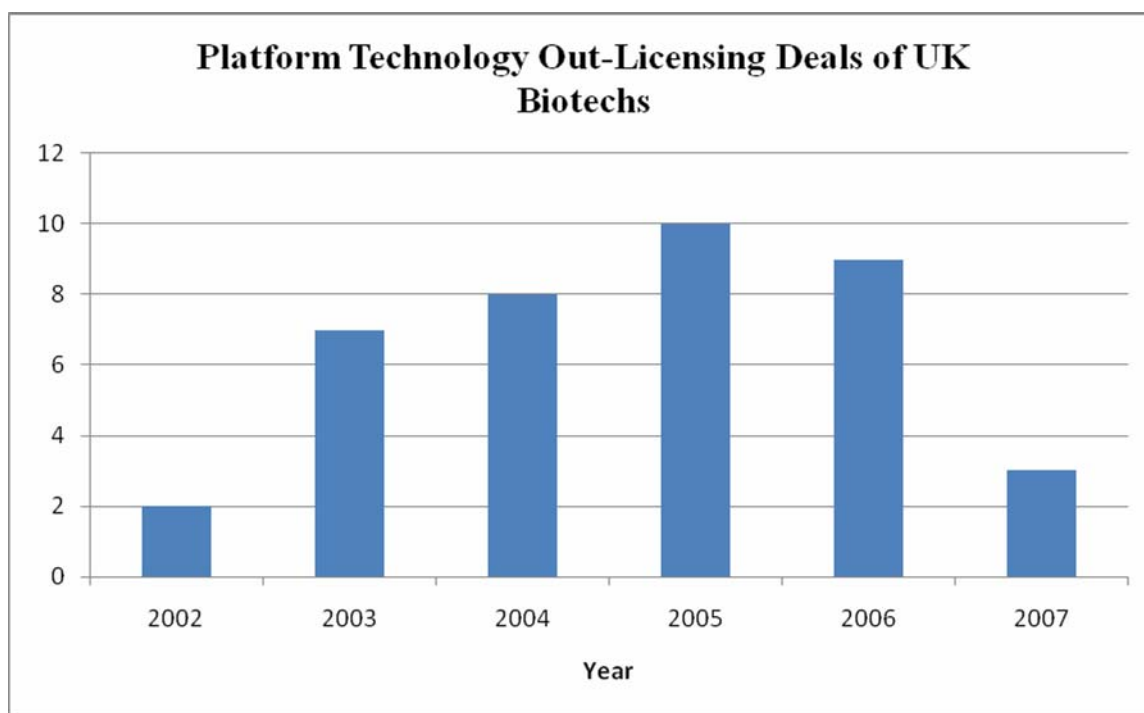


Figure 11 Platform technology out-licensing deals of UK biotechs

The ‘salami-slice’ strategy in performing non-exclusive out-licensing deals was seen in UK biotechs that develop platform technologies. Such strategy not only maximises the available revenue streams, it also reflects validation of the small biotech’s technology being applied in the pharma’s drug discovery processes.

The peak in technology platform out-licensing activity also coincides with the increase in early-stage licensing deals. A plausible explanation for this trend is that with relatively few late-stage targets available for in-licensing, pharmaceutical companies were investigating into both early-stage innovations and into gaining access to platform technologies. These technologies are applicable to a wide variety of product opportunities to support the growth of pipeline. However in last year, pharmas had shown declining interest in in-licensing platform technologies and it would be worthy to note what factor had brought about such a change.

3.2.2 M&A Trends

More M&A deals had happened on a much smaller scale

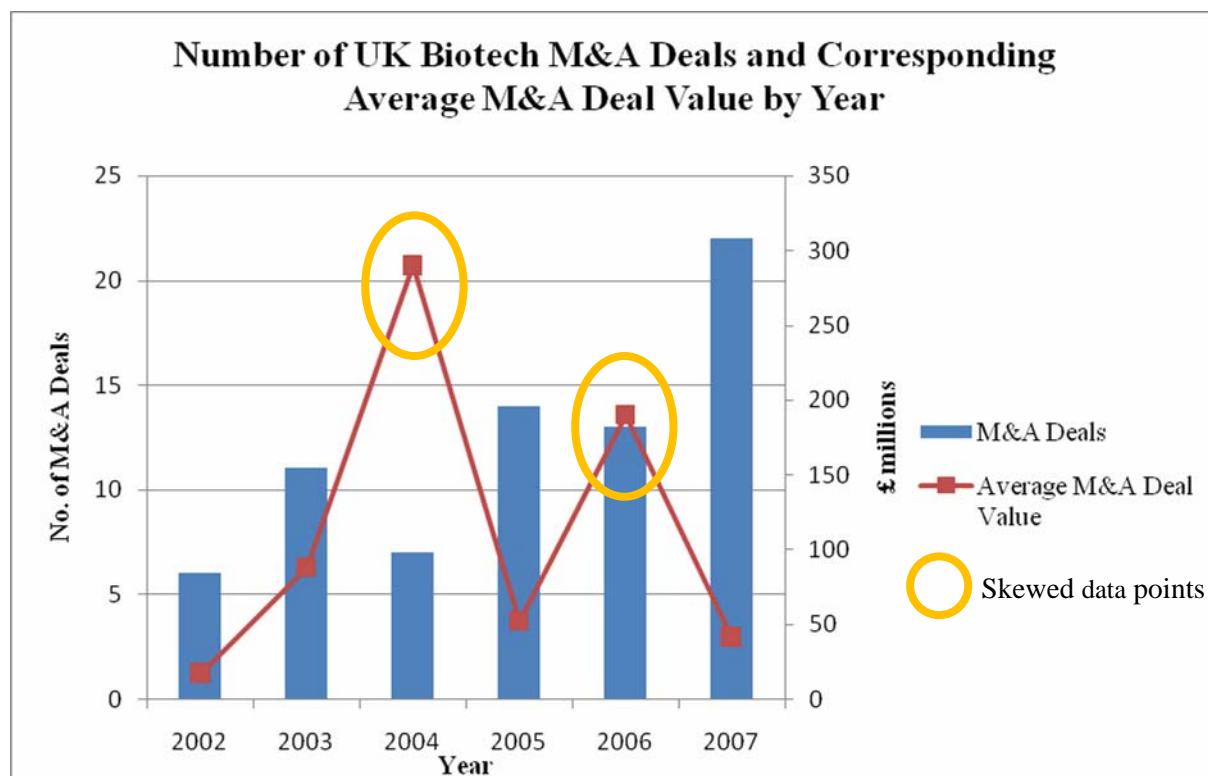


Figure 12 Number of UK biotech M&A deals and the corresponding average M&A deal value by year

The average M&A deal value was skewed in 2004 and 2006 because of one or more unusually high premium M&A incidents. When not including these two data points, the average M&A deal value has not increased too significantly over the years. In early 2002-2005, pharmas started to hunt around for late-stage alliance opportunities to replace the in-house late-stage products that had run into various set-backs, which saw the gradual rise in both licensing and M&A deals. Pharmas had seen the need to rebuild its discovery capabilities and to focus on devising longer term strategies. However the UK biotech sector has only a limited supply of these opportunities and these deals started to deplete in numbers. During 2006, the most attractive UK biotechs had been acquired with significant premiums. By 2007, the appetite of the big pharmas had then grown to take up much smaller entities with lower enterprise value.

Active consolidation activities is taking place in the UK biotech sector

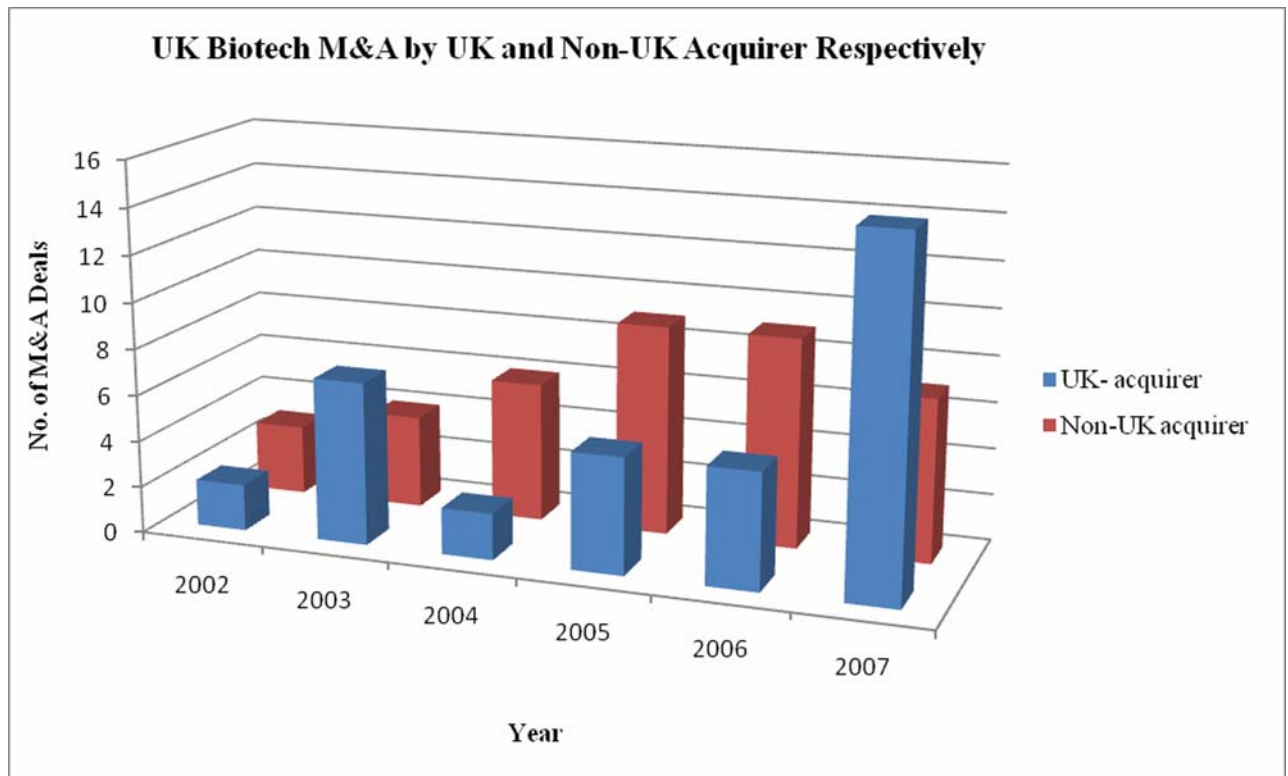


Figure 13 UK biotech M&A by UK and non-UK acquirer respectively

At the same time, the UK biotech sector has undergone some degree of consolidation as exemplified by Oxford Biomedica's acquisition of Oxxon Therapeutics and Serentis's acquisition of Surface Therapeutics. Whilst the model of a large number of weak companies in the UK biotech sector is not sustainable, combining high-quality biotechs to strengthen R&D capabilities and in-house pipeline would have a better chance of survival when competing against emerging biotech regions in Continental Europe and Asia.

Conclusion

From the above analysis, the main findings are as follows:

- There was a general increase in alliance activities in the UK biotech sector but M&A activity had outpaced licensing activity in 2007
- The averaged 'bio-value' in licensing deals had grown mainly due to the adaptation of back-end loaded licensing strategies
- There were more M&A deals in numbers which happened on a much smaller scale

These observations have confirmed the initial proposition of the increase in licensing deal values and there was indeed a slight inclination for pharma to acquire than to license. The main point of consideration taken to choose one over the other is the financial risks that have to be undertaken, which are further explored in the following chapter.

Chapter 4: Selected Case Studies

These case studies are set out to find the risk-adjusted net present value (rNPV) of the licensing deals. The valuation model also provides us with a measure to illustrate how the value of a particular licensing deal is shared between the licensor and licensee respectively, and in turn to extrapolate corresponding justifications from the pharma's perspective to choose licensing over M&A in these scenarios.

4.1 Basis of Selection

The case studies selected were the most prominent licensing examples in the UK biotech sector during 2005 and 2007. There are more detailed breakdowns of deal terms available as public information in the press releases or from the respective company's annual report. Therefore, the degree of estimation required to perform the rNPV analysis for each licensing deal can be minimised. Summary tables for the terms of the four chosen licensing deals are shown in **Appendix 3**.

4.2 Valuation Methodology

The announced bio-value of the licensing deals is the sum of all upfront payments, milestones (development and sales) and in some cases, royalties upon net sales. It is a simple cumulative value of the licensing deal as it does not take discounting into perspective, in which case the projected cashflow from future milestone/royalty payments are supposedly worth less today. Moreover, the bio-value corresponds to a non-risk-adjusted value where the inherent high risks of failure in the development process are not accounted for, e.g. technical and scientific risks, regulatory risks in clinical trials and in achieving marketing approval. Hence the risk-adjusted net present value (rNPV) method is used in order to value the licensed product in today's terms, as well as to reflect the development risks incurred as the product progresses through clinical trials.

The rNPV first considers the cash flow of a development project which include all relevant costs (R&D, marketing) and revenues (sales). The project is appraised over a period of time, encompassing the product's full lifecycle from its current stage of development to its eventual post-patent sales¹¹.

When the product has received marketing approval, the product's life cycle is adopted from the Lehman Brother's report as it provides a good estimate for the future revenues generated in subsequent years post-marketing. The F2 curve (**Figure 14**) was chosen because it corresponds to typical product characteristics of biologics¹² (Lehman Brothers, 2004).

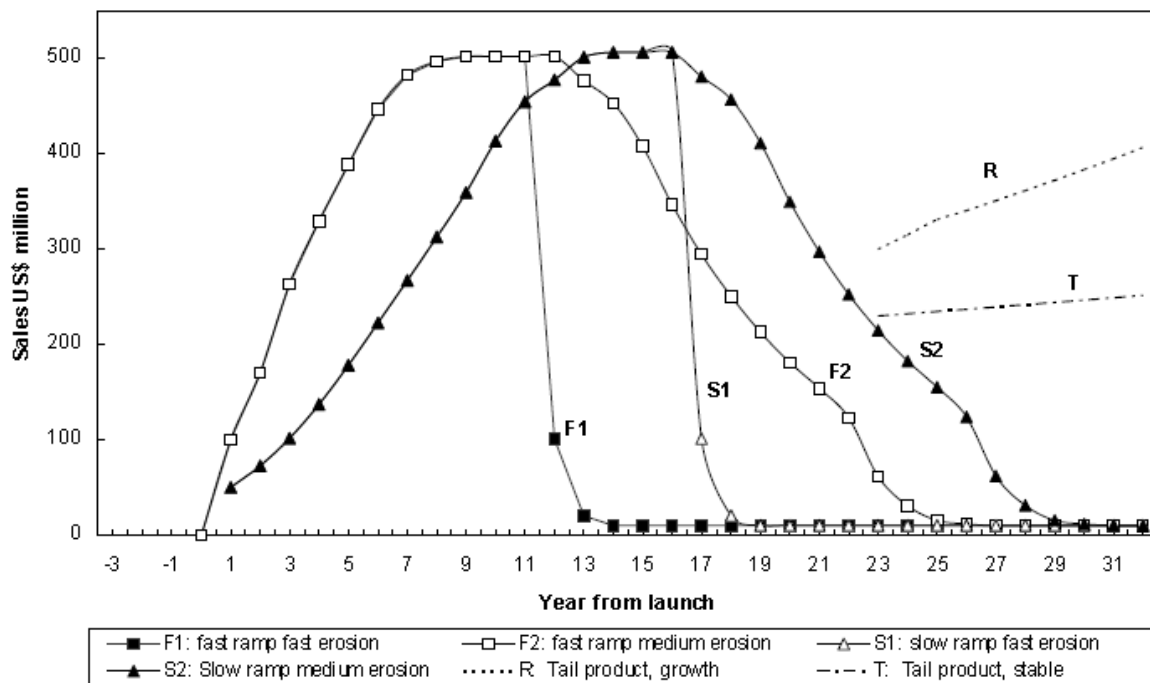


Figure 14 Life cycle revenue curves (Lehman Brothers, 2004)

¹¹ Phase II development of the project is scheduled to last two years, followed by three years in Phase III development. The application for regulatory approval is then submitted, with the approval authorised in the following year.

¹² F2 curve represents a fast ramp-up to peak sales and reaching a plateau after 8-10 years. Erosion in sales is much slower where the gentle decline is due to product obsolescence or by multiple patent expiries in different regions.

Product attrition rates (**Figure 15**) are then applied to adjust the cashflow with different probabilities of success at these different stages of development. The cashflow is then discounted at an appropriate rate. For the purpose of this study, a discount rate of 15% is used in all cases since it is considered to be a typical rate used in the industry (Puran, 2005).

	Probability that the average product will:		
	Make it all the way to market	Make it to the next stage	Cumulative
In preclinical	3%	38%	100%
In phase I	8%	40%	38%
In phase II	20%	54%	15%
In phase III	37%	45%	8%
In registration	82%	82%	4%
Launched	100%	100%	3%

Figure 15 Product attrition rates¹³

The rNPV is the value for the whole project in which the licensee and the licensor each gets a share of this value according to the financial terms specified in the licensing deal. The licensee most often bears all cost for further clinical and regulatory developments plus the marketing cost unless stated otherwise. Their expenses also encompass the milestone payable to the licensor at the end of each successful stage of the development and royalty payments upon net sales.

¹³ Source: Tufts Institute, ING estimates, CH&B estimates

Royalty rates

In cases where the royalty rates were not stated, published net royalty rate (**Figure 16**) is used as the basis for the estimation of future revenues generated¹⁴. For the licensing deals where the licensors are also receiving sales milestones, the full royalty rates are not used in these cases but are discounted from 15% to 3%. This is because although royalty payments and sales milestones are paid under different sets of conditions, they would ultimately contribute to the total amount payable upon sales-related performance.

Product Status	Net Royalty
Discovery	Nil
Preclinical	4%
Phase I	10%
Phase II	15%
Phase III	25%

Figure 16 Risk and return profile for drug development

(The Allen Consulting Group, 2006)

The cashflow of the licensee is thus the total revenue generated from the sales of the product minus the total expenses and this amount is risk adjusted before discounted to yield the rNPV of the project to the licensee. The rNPV of the project to the licensor is yielded in a similar way. An example spread sheet showing the valuation of one of the case studies is shown in **Appendix 4**.

¹⁴ Where an escalating royalty rate is stated in the licensing agreement, the royalty rate is approximated to be proportional to the percentage of peak sales achieved as set in the F2 Lehman Curve.

4.3 Discussion

Using the risk-adjusted discounted cashflow model, the rNPV and the relative value distribution between the licensee and the licensor are shown in **Figure 17** and **Figure 18**.

Product (Licensor/ Licensee)	Phase of development	rNPV of project	rNPV for licensee (% of project rNPV)		rNPV for licensor (% of project rNPV)	
			Excluding royalties	Including royalties	Excluding royalties	Including royalties
TroVax (Oxford Biomedica/ Sanofi-Aventis)	Phase III	£405m	£344m (85%)	£250m (62%)	£61m (15%)	£155m (38%)
CytoFab (Protherics/ AstraZeneca)	Phase IIb	£172m	£124m (72%)	£75m (43%)	£50m (28%)	£98m (57%)

Figure 17 rNPV and relative value distribution of licensing case studies without sales milestones: i) Cytofab royalty: 20% (stipulated); ii) Trovax royalty: 25% (standard)

Product (Licensor/ Licensee)	Phase of development	rNPV of project	rNPV for licensee (% of project rNPV)		rNPV for licensor (% of project rNPV)	
			Excluding royalties	Including royalties	Excluding royalties	Including royalties
Juvista (Renovo/ Shire)	Late Phase II	£172m	£100m (58%)	£95m (55%)	£72m (42%)	£77m (45%)
AS 1404 (Antisoma/ Novartis)	Late Phase II	£125m	£68m (54%)	£63m (51%)	£57m (46%)	£62m (49%)

Figure 18 rNPV and relative value distribution of licensing case studies with sales milestones: 3% royalty

Despite the fact that these products were at relatively late-stages of their development and much of the development risks had been taken out, the pharmas were still able to capture substantial value from these licensing deals, ranging from 43% to 62% of the rNPV with royalties included as part of the expense.

Development risk is probably the biggest impeding factor to acquisition

In these 4 cases, the pharmas considered licensing as the better option to secure their interest. With hindsight, 3 out of the 4 of products had suffered different scales of developmental setbacks since the licensing agreement was made^{15,16,17}. By acquiring the biotech entity instead of in-licensing the major product means that the pharma is taking onboard full development risk at a much high cost. Therefore, product attrition alongside with the possibility of their huge investments ending up in a blind alley, are indeed very significant impeding factors to acquisition.

¹⁵ CytoFab: a new mid-stage trial was planned which would take another 21 months to complete. The intended launch would possibly be delayed. New trial for CytoFab as investors urge action. 2nd November, 2006.

<http://www.fiercebiotech.com/story/new-trial-for-cytofab-as-investors-urge-action/2006-11-03>

¹⁶ Juvista: failed to reduce scars in its phase II studies, which had led Renovo's share price to fall 51% following the announcement . Renovo Falls on Juvista Failure in Breast-Scar Trial. 3rd March, 2008. http://www.bloomberg.com/apps/news?pid=20601102&sid=aOOSIMd_aWFE&refer=uk

¹⁷ AS1404: failed to show effects in treating in one of its planned indications (ovarian cancer) and Antisoma's share price fell by 17.8%. Antisoma shares freefall on drug failure. 12th July 2007. http://business.timesonline.co.uk/tol/business/industry_sectors/health/article2064553.ece

Value of product of interest versus strategic fit of baggage assets

In the licensing deal for CytoFab, AstraZeneca (AZ) made a £7.5million equity investment, equating to 4.3% of Protherics' enlarged capital in the company. Assuming that the premium being paid was a fair justification of Protherics' market value at the time when the investment was made, it can be postulated that AZ would pay a conservative estimate of £175million to acquire Protherics otherwise. With the rNPV yielded for CytoFab valued at £172million, in a sense AZ could have acquired the rest of Protherics' assets at only a small extra cost.

Apart from the development risk, a probable explanation for AZ not opting to acquire is that AZ had not substantially been involved in critical care and Protheric's key strengths would not dovetail with AZ's existing capabilities and pipeline. Further investments would be required to allocate new resources to manage other early stage, high risk cancer therapeutic products from Protherics' pipeline. In-licensing allows AZ to buy into opportunities in a new therapeutic area by paying a mere £25m upfront, and further investment can be de-risked by paying milestones only on a contingent basis.

Appropriate size for acquisition

Using similar calculations, it is estimated that Shire would need to spend £354m to acquire Renovo¹⁸, whereas the rNPV of Juvista is worth £172m. This illustrates that Renovo has a lot more asset value than Juvista itself, and licensing the single product would be much cheaper than buying up the whole entity. If Shire was to pursue acquisition, immense resources would be required to handle post-M&A integration and reorganise the baggage assets.

¹⁸ Shire made a £25 million equity investment in Renovo at a subscription price of £2 per share, which represents approximately 7% of Renovo's share capital.

Licensing provides better insight to the biotech's potential

The rNPV of Trovax is £405m, whilst the estimated acquisition cost of Oxford BiomMedica based on the market capitalisation at that time at a 50% premium¹⁹ is £425m. The rNPV might suggest acquisition was a feasible alternative, but rNPV remains a considerably optimistic estimation because it comes with constraints that Trovax has to be able to treat in all three indications²⁰. Nonetheless, with Trovax developed to potentially treat any cancer type, it still presents immense commercial potential to fulfil unmet medical needs. Together with the appealing broad portfolio of late-stage and early-stage products, Oxford Biomedica is an attractive acquisition target. Acquisition is crucial for Sanofi-Aventis to maximise their return on investment because downstream payments would significantly erode the value attained from Trovax (~23%). By in-licensing, Sanofi-Aventis could probe into the biotech's IP assets and wait for more significant validation from the continuing clinical trials.

Another example that supplements the argument of “license before acquire” is the licensing agreement between Antisoma and Novartis. Licensing allows Novartis to attain 51% of the value in AS1404 (now known as AS404) in a de-risked model of a back-end loaded deal, comparing to the acquisition expense of £305m at 30% premium. Licensing allowed Novartis to gain exclusive access to AS404, but AS404 is only one of the promising lead clinical products for the cancer treatment in the portfolio. In longer strategic terms, if AS404 or any of Antisoma's clinical products could achieve further clinical inflexion milestones, it would be sensible for Novartis to acquire the entity to secure these opportunities²¹.

¹⁹ Acquisition premium is a fair estimate based on biotechs with similar platform technology capabilities and broad pipeline, such as that in the acquisition of Cambridge Antibody Technology at 60% premium

²⁰ Trovax: ongoing clinical studies in renal cell carcinoma, colorectal cancer and prostate cancer; further potential application in a wider range of other solid tumours, including lung and breast cancer.

²¹ Report from KBC Peel Hunt in Jan, 2008 comments “Antisoma will be ripe for acquisition toward the latter part of 2008 as AS1402 and AS1411 become more attractive to other blue chip pharma companies, which we believe will force Novartis into making the acquisition before the ASA404 data is announced.”

Conclusion

The above case studies illustrate the various financial concerns between licensing and acquisitions. For a single-asset biotech, the rNPV for its key asset is very close to the capital needed to acquire the company at the current market valuation of the biotech. However, licensing of a single product is much cheaper to pursue because

- Licensing de-risk investment through milestones payments payable only on a contingent basis and can be allocated to further downstream royalties
- Licensing is a more effective route to gain access to a single product of interest in a relatively large biotech entity
- Licensing allows the pharma to gain validation to the biotech's technological assets and to overcome significant developmental hurdles before deciding upon acquisition

On the flipside, licensing can only be effective to a certain point before other factors kick in, such as competition for the asset and downstream financial burden in back-end loaded licensing deals. Under such circumstances, acquisition would be the recommended strategy providing that the biotech is appraised at a reasonable value.

Chapter 5: Interview Analysis

5.1 Participants

The interviews were conducted within the inclusive period from 29th April, 2008 to 16th May, 2008 in conjunction with Cambridge Healthcare and Biotech. Individuals were selected from the company database, with participants based in UK representing biotech business development (biotech), large pharma business development (pharma) and venture capitalists (VC). A total of 28 individuals were approached and 12 agreed to be interviewed. Seven interviews were face-to-face and the remaining five were telephone interviews for logistic reasons.

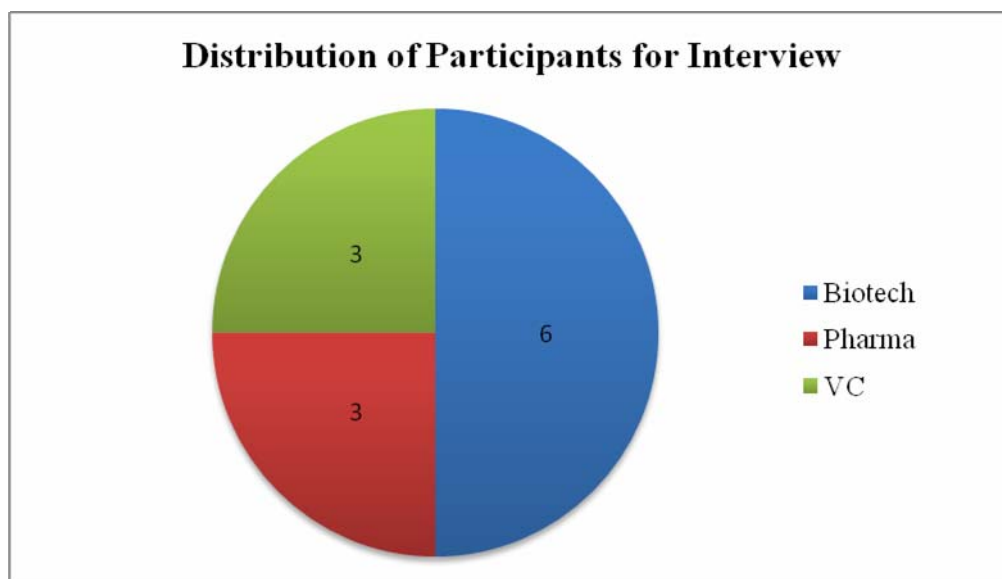


Figure 19 Distribution of participants for interview

Three different sets of questions were designed to target the specific groups of interviewees (refer to **Appendix 5**) and to act as a general guideline to identify key areas of interest with the following objectives in mind:

- i) To identify the major drivers for pharma’s strategic choice of acquisition
- ii) To understand how the pharmas capture value in licensing opportunities with small biotechs
- iii) To understand what are the factors that contributed to the change in licensing trends
- iv) To understand what are the rationales behind VC’s decision processes upon exit routes for their portfolio biotechs

The interviewees were also invited to comment on Figure 6 to Figure 13 in Chapter 3. The most prominent M&A deals that were mentioned by the interviewees are shown in **Figure 20**. The high profile acquisition values raised awareness and there were specific assets that the pharma acquirers were interested in.

Target Company	Acquirer	Value
Cambridge Antibody Technology	AstraZeneca	£702m
Domantis	GSK	£230m
PowderMed	Pfizer	£178m

Figure 20 Top UK biotech M&A deals in recent years mentioned by interviewees

5.2 Findings and Discussion

5.2.1 M&A Trend Analysis

Drivers for Growth in M&A

In general, the underlying reasons for pharmas to acquire are very much in line with previous discussions. The most potent driver of M&A is to enter a new area where the pharma has not previously been involved, and M&A is seen as the quickest mechanism to achieve this. To a lesser extent, there was also a need for the pharma to expand their presence in a foreign market by integrating the smaller biotech into existing structure.

For pharmas, the major selection criteria of the suitable acquisition target are as follows:

- i) **Financial fit:** the net worth of the biotech plus the acquisition premium has to be well justified and within budget
- ii) **Strategic fit:** pharmas look for products that can fit into their pipeline or well proven technologies that can be incorporated into a discovery asset
- iii) **People fit:** the human asset, particularly the R&D capabilities, is of concern because it affects the post-merger integration of the acquired entity

With reference to the previously discussed trend findings, there were more M&A deals than licensing deals for the first time in 2007. Some interviewees had put forward further plausible reasons that had promoted such drastic growth of M&A deals in the UK biotech sector.

i) ‘Fear mentality’ forces pharma to acquire

The increase in M&A activity was interpreted by a few interviewees as the pressing urgency of the pharmas in making a bolder strategic move other than in-licensing. In some cases if the pharmas want security for a particular favourable asset, acquisition of the small biotech is the only remaining strategic option.

“Abgenix (taking away) from AstraZeneca part of their antibody platform is one of the things that probably influenced their option to buy CAT (Cambridge Antibody Technology) apart from having done the licensing deal originally... so (acquisition) guarantees that they get to internalise the bit of technology without someone else running away with it under their noses.” (biotech)

Nonetheless, as there are fewer end-to-end biologics players left for acquisition, there is a presumed likelihood that the growth in biotech M&A will persist because competition will force big pharmas into serial acquisition before emergence of a bidding-war.

ii) Acquisition can be cheaper than licensing

The fact that licensing deals are getting more expensive due to competitive bidding makes acquisition of the small biotech cheaper than to in-license multiple products of interest. This is compounded by the less generous market valuation of small biotech public companies, where the net present value (NPV) of the cashflow required from the pharma to fund the clinical trials in a licensing deal is quite often a substantial proportion of the small biotech’s whole market capitalisation. Therefore, these companies with a weak balance sheet become easy acquisition targets for big pharmas.

In certain cases, progressing onto acquisition makes more economic sense for the pharma rather than to pay the ongoing financial burden of contingent milestones and royalties.

iii) Lack of options for small biotechs where the VCs need to exit

Exits for small biotechs under the current economic downturn are becoming more difficult and less profitable for investors. As VC companies are getting to the end of their fund cycle, they may have greater intention to exit.

“I think that the increase in M&A deals are probably as a result of the fact that there were quite a few of companies who had been in existence for quite a few years and have gone through several rounds of private financing, but are no longer sustainable anymore. They are unable to raise public financing through IPO, so they are forced into the M&A route.” (VC)

“We have the pressure on ours to exit, but that doesn’t mean that you can exit even if you have the pressure. It’s a function of what the market wants and buys.” (VC)

One of the pharma interviewees indicated that at times he felt pressure to turn the initial licensing transaction into acquisition when involved with VC controlled biotechs. Nonetheless, the M&A exit route for a biotech is reliant on how well the match is between corresponding assets in the biotech and the needs of the pharma.

5.2.2 Licensing Trend Analysis and Corresponding Strategies

Licensing is the preferred option, acquisition is the last resort

Licensing is perceived as a more effective way for the partners to share development risk and where complementary abilities can be fully utilised. The investment for licensing is segmented such that more cash is paid only when there is a higher certainty that the product or technology is feasible. Conversely, acquisition requires much larger upfront investments with higher associated risk. Pharmas are cautious regarding M&A and they would wait for as long as they possibly can before acquisition becomes inevitable.

*“The most likely situation that we would consider acquisition is when the small company has a valuable product in hand, but it does not have the money to last for a further year or two and would go into bankruptcy otherwise....**You either lose it or buy it.**” (pharma)*

“People were racing to put down assets in the biological space. It’s a little bit like the nuclear arms race...It’s undoubtedly true that the pharmas respond to what they perceive as competition to buy.” (VC)

Acquisition requires a lot of management time to be invested in the process itself, and even more is needed to take care of the peripheral issues that are beyond the scope of simple financial expenses. One might want to integrate the development group from the acquired entity within its own research team, but this also depends on the size of the acquired entity and cultural fit. Therefore acquisition can only cut cost up to a certain point, whilst licensing is a more flexible alternative to achieve a less ambitious goal.

Increase in licensing activity is driven by the pharma's need to externalise

Amongst the pharma interviewees, there was consensus upon their need to externalise through licensing. The traditional pharmaceutical model with the long standing focus on large primary care market is failing and so they are eager to search for innovative, more targeted medical interventions through broad external partnering with biotechs. The screening criterion for the ideal licensing opportunity varies, but generally pharmas are more adventurous to in-license early-stage products in therapeutic areas in which they are already active, so as to complement their existing portfolio of molecules. They also capitalize on their experience in identifying the associated risks involved further down the clinical development timeline and the intrinsic novelty required to differentiate such molecule from existing therapies. In contrast, pharmas would seek late-stage in-licensing deals in areas in which they are not as involved. The ideal in-licensing candidate would have to show supreme clinical data and be ready to market within a short period of time.

Licensing is part of due-diligence for acquisition

The initial licensing relationship is seen as a form of due-diligence and can therefore lead to a smooth transition to acquisition. Therefore, the increase in licensing alliance might have guided the subsequent increase in M&A deals. By making a substantially smaller commitment comparing to M&A, pharmas can make a better assessment into the technological and cultural fit of the biotech. In being a licensing partner, the pharma has also a higher chance in succeeding quicker acquisition ahead of fellow competitors that may become interested in the targeted biotech.

“...we already have an arrangement with the company, i.e. we are already licensing one of their products. If things go well, we like the company, we would buy the company.” (pharma)

Increasing bio-value may not equally imply the increase in asset valuation

There is a general impression amongst the pharma interviewees that fewer development projects are available and the growth in the bio-value had mainly been in the relatively late-stage projects. However as most of the attractive projects have already partnered, the appetite for the pharmas to identify potential partners has grown to such that even early-stage projects are attracting higher value. Thus the licensing premiums are largely driven by **competition** as well as the pharma's **willingness to pay**.

Although the 'bio-value' is arguably the best available indicator for the size of a licensing deal, it does not necessarily depict the true value of the deal. When asked about the interviewees' perception of bio-value, all biotech interviewees remained skeptical about the value. The bio-value is useful to raise shareholder's interests or to gain credibility within the biotech partnering arena, but what matters the most to both partners is the amount of upfront being paid.

“The moment I look at this number (bio-value), I automatically apply a massive discount...You really don't know what's behind the number as there might be a lot of manipulation.”(biotech)

Bio-value is a very big lump-sum figure including both upfront and milestones. The increase in bio-value is entirely driven by the increase in milestones causing the licensing deal to be progressively back-end loaded. Pharma as the licensee would aim to de-risk its investment by allocating more attractive downstream milestone payments and royalties in exchange for lesser commitment upfront. Pharmas might just be more lenient in granting higher royalties because they would acquire the biotech before being encumbered by the heavy downstream payments. In a way the increase in bio-value might not adequately illustrate the influence from other value-drivers.

“I believe that the pharmas or the big biotechs will agree to big downstream, knowing that they will never have to pay them because they will buy the company if they succeed.” (biotech)

Licensing: weighing between pros and cons

Engaging in licensing deals is a vital way to raise financing for small biotechs. The greatest jump in value for out-licensing deals perceived by interviewees is at Phase IIa, where the product can validate its potential by gaining clinical proof-of-concept. Small biotechs often do not have cash, experience or capabilities to bring the product further into clinical development, therefore out-licensing is their best option to extract maximum value with minimised risk.

Conversely, the downside of out-licensing is that it could detract the future option of a trade-sale. By out-licensing their most crowned assets, small biotechs would diminish their attractive takeover prospects and compromise on their negotiating leverage with their potential acquirer.

“...a licensing deal makes you unsellable, because the perception is that you don’t have a real value product other than the one that is being out-licensed, then (because otherwise) the big company would have bought you. But on the other hand the right licensing deal can be transforming to the company, providing validation of the technology to the outside world.”(biotech)

The main challenge for a biotech is to devise an appropriate strategy that can lengthen their existence whilst keeping future partnering options open by maintaining control of key intellectual properties. As a licensor, the biotech always demands for as much upfront as possible; but the general impression gathered is that it is getting more difficult to do so.

5.2.3 The role of VCs in driving biotechs towards M&A

General perceived dynamics in the UK biotech market is poor

As a high capital consumptive business, biotechs have to raise money either from the investors or pharmas. Unfortunately at present, the amount of financing that can realistically be raised from the public market is minimal in comparison to the amount required to establish a revenue-generating pipeline. Collaborative alliance with big pharmas is an effective way of raising non-dilutive financing for small biotechs, and it is increasingly the more fashionable choice.

“I wouldn’t want to be trying to raise money for discovery company today, not in this country. I don’t think you will find the funding.” (biotech)

“There is obviously a disconnect between what the company think it’s worth, and what the public market thinks it’s worth.” (biotech)

Even though the US biotech market is not thriving at the moment, it has more depth of quality businesses and funding in contrast to the UK market. The NASDAQ has sufficient numbers of public biotechs that investment houses are prepared to spend resources on dedicating teams to advise non-specialist investors upon their investment options. Conversely, with the inherent fragmented nature of the European biotech sector, the regional number of biotechs being floated is much smaller. There are fewer resources devoted to monitoring the activity in the biotech sector, resulting in UK biotechs being undervalued relative to their US counterparts.

“I think some companies have gone public too early particularly on AIM...Some of the investments are suffering because they have investors that don’t understand the sector and don’t appreciate how long it takes to develop the products.” (VC)

The net result of such pessimism in the UK biotech market has meant that capital flow has not only stopped at the top, it has also stopped from the lower end of the funding chain. Investors are not prepared to fund businesses when exits cannot be secured and such limitations would perhaps stunt the growth of the UK biotech sector.

IPO window is closed, so M&A is a more reliable exit for VC

As agreed by all of the interviewees, the near-term outlook of the IPO market is not optimistic, but it is believed to be only part of the cyclic behaviour. Market capitalisation is very depressed and it does not seem to bear any resemblance to the actual asset value of the company, so it is very difficult for private companies to achieve high valuations at IPO. Furthermore, IPO does not offer the liquidity that VCs require because the process involves either 6 or 12 months of lock-in period, in which investors who invested during the private rounds are restricted on when they are allowed to trade. When the lock-up period has ended and they intend to sell their shares, the return may no longer be optimal because share price fluctuates under market uncertainties.

“Most stocks, certainly in the UK, when they go public, they then decrease...if you look at 6 months to a year, most of the stocks are valued less than their IPO price.” (VC)

“I have a very negative view on the IPO possibilities for any UK biotech company in the UK...I don’t think that UK market at the fund manager level has any appetite at all for biotech stocks.” (VC)

Knowing that the UK IPO market for biotech is more or less closed, VCs have imposed a stronger stance from where the alternative exit is most likely to come from. With the British pounds going strong, it is difficult to go geographically outside of the UK to gain access to capital. Hence, the only remaining realistic exit is through trade-sale.

However, being reliant on the trade-sale route is impractical because the decision to buy is often out of VCs’ control. Value of a small biotech M&A is the value that the pharma is prepared to pay, so this is dependent on how desperate the pharma needs it. Pharmas are more likely to pay a much higher premium in cases such as AstraZeneca, where their need was to jumpstart its biologics pipeline through acquisitions.

VCs press to exit at the end of their fund cycle; they may also groom for acquisition right at the start

The pressure for the VCs to exit escalates as the stage of the small biotech gets closer to the end of the fund cycle. However the effectiveness of such pressure also depends on the funding status of the biotech (whether it is a cash-leaking asset) and other external market factors such as competitive tension.

“If the company is a distressed asset, then you can probably buy it for so cheap that it would actually be cheaper than licensing.” (biotech)

“VCs can push more to an exit, but it’s harder if you are pushing from the inside...than if that external party has already taken a view around the sector and see that competitive pressure is around their peer group and (that would) start to impact upon them.” (VC)

Exit option is one of the top priorities that VCs have to consider before making their investment, and it was shown that some would also plan well-ahead to keep a potential buyer interested. A VC interviewee indicated that they would work with pharmas to identify the companies they would want to acquire in the long-run, and hence invest in these companies ahead of the pharmas. By tailoring the growth of the biotech according to the pharma’s need, VCs can rationalise the high acquisition premium. In that way VCs would be able to secure an exit for their portfolio company well before the end of their fund cycle.

“I would call the business development and scientific teams in the pharmaceutical companies and ask them what they are looking for... I do that before the deal is done. And once the deal is done, I meet with the pharma people regularly to make sure they are updated on the company’s (biotech) development. So when there is an acquisition, they already know the company very well.” (VC)

Valuations of UK biotechs remain comparatively high from VC's point of view

From the general impression gained from VC interviewees, current biotech valuations range from being medium to high, but this varies between different subsectors. Naturally, a slightly contrasting view is perceived by the biotech interviewees where they think that the present valuation of the UK biotech sector is currently better justified than it was previously and that they had been undervalued a few years back. Nonetheless, one of the VCs pointed out that valuation has been high not only because of the capital intensity in the UK biotech sector, but also because the British pound is strong in comparison to other currency.

As agreed by some interviewees, the nature of academic strength accompanied by their successes in spinning out IP has enabled the UK biotech sector to develop to a relatively mature phase. Therefore, companies that are equipped with attractive products and/or a track record of providing proven platform technologies present massive opportunities for pharmas to partner with. In spite of this, and as biotechs in other European countries are now getting to the stage of maturity that the UK biotechs had achieved a few years ago, the strength of the UK biotech may no longer present the same attractiveness to investors.

“Many UK VCs go into continental Europe and invest because valuations are typically more competitive and therefore one can potentially make better returns on exits.” (VC)

The bars are raised for early-stage biotech ventures to achieve success

The near-term venture funding outlook for biotech startups might not be too hopeful, but it does not mean that there is no opportunity to be grasped. According to the VC interviewees, the current focus to build a successful early-stage biotech business is to achieve **capital efficiency**, with clear value propositions, value increment points and exit strategy. VCs tend to keep a tight control on the cash investments into the biotechs through tranche financing. Incorporating additional sources of non-dilutive capital from alliance partners is critical to help lengthen the period of time before another round of capital needs to be raised.

“Venture is something that plays better off being opportunistic. (It is about) seeing high quality ideas and teams and being able to back them with significant amount of money on an opportunistic basis rather than on a pre-determined basis.” (VC)

The occasion to float a biotech in the IPO that can sell shares at high prices is only feasible for certain companies with attractive late-stage products, along with strong alliance deals and financial support from big pharmas. On the other hand, some interviewees feel that M&A is likely to increase because there is a need for some level of rationalisation and consolidation to happen in the UK biotech sector, where early-stage companies get together to fund a de-risked model with a number of different products to create a more sustainable future.

“It (M&A) actually needs to happen in biotech... Having lots of very small companies doesn't necessarily create companies that are well positioned to compete on a global basis.” (biotech)

“Consolidation should happen before an IPO...with the current climate and liquidity crisis, it's bound to disappoint, unless it's a very good product.” (biotech)

5.2.4 Conclusion: is it Better to License or to Acquire?

There is no generalised, clear-cut answer as to whether licensing or acquisition is the best strategic option for a big pharma because such decisions are determined on a case-to-case basis. As this is a multi-dimensional problem, the ultimate verdict should not be solely based on financial considerations. The inherent risk profiles are dissimilar in licensing and acquisition and therefore they cannot be directly compared with one another.

- Acquisition involves a much larger upfront investment than licensing and the acquirers have to bear all uncertainties about the future development of the targeted biotech.
- Licensing allows risk mitigation through tranche milestone payments and eliminates the need to integrate any liabilities attached to the acquired entity.

It is important for the pharmas to first identify the specific assets that are being sought after in the small biotech and to survey the competitive landscape before making a fair judgment on whether it would be cheaper to license or to acquire.

To a greater extent, the value of the biotech's assets is also dependent on what the investors and the general market perceive it to be. At the same time, VCs also play a significant part in dictating the growth of UK biotech sector by influencing investment trends. There has been more focus to achieve capital efficiency in small biotechs and licensing is seen as an important source of non-dilutive financing. VCs experience higher pressure to exit as they get nearer to the end of their fund cycle, but their return on investment is highly dependent on the market status. Knowing that the UK IPO market is not optimistic, VCs have imposed a stronger stance on the trade-sale exit for their portfolio companies.

Undoubtedly, acquisition is a vital exit for the investors in the small biotechs, but it does not necessarily benefit the company's future. Post-acquisition integration is of high importance in maximising the core value attained through M&A. As mentioned by a few of the interviewees, destruction of value is a common dilemma when integrating an entrepreneurial biotech into a big pharma's bureaucratic structure. Therefore, a more appropriate operating model might be to allow more independent growth so as to preserve the creative dynamics within the entity.

Chapter 6 Strategic Recommendations

In order to improve their earnings, pharmaceutical companies not only have to cut internal costs but must also make more radical changes to their externalisation strategy. In return for their innovative impact on enhancing big pharma's productivity, the small biotech can take advantage of such collaboration to increase flexibility and capitalise on the value of their assets.

6.1 Strategic Recommendations to Big Pharma

The most effective partnering strategy differs on a firm-specific level and the decision is also strongly influenced by the prevailing market condition, but in general the following points of consideration are gathered as a result of this study.

- i) It is **preferable to license** if the pharma is only interested in one product because the remaining peripheral assets in acquisition require enormous time and effort to resolve. Composition of a back-end loaded licensing deal can also minimise the investment risk within an unfamiliar therapeutic area.
- ii) With the IPO exit as a less viable option under current economic downturn, VCs would experience greater pressure to exit through M&A as they are reaching the end of the fund cycle. However they would still demand high returns on their investment with a fair value assessment according to current market value, and it is fair to say that valuation of UK biotech remains on the high end of the scale.
- iii) It is **preferable to acquire** if the pharma is interested in a portfolio of products and/or technology platform in the small biotech, because the risk of acquisition is diversified without banking the whole spending solely on one asset. Acquisition becomes inevitable in particular areas where there is high intensity competition for the specific assets. Competitive tension is likely to intensify because the available acquisition targets are depleting in numbers.

- iv) Acquisition of a private biotech may allow a more creative type of M&A deal to be structured such as that with an earn-out arrangement. The biotech can be bought with an initial modest premium, and then further premium can be paid to the shareholders at certain contingent milestones.
- v) In post-acquisition, it is possible to spinout or to divest assets that are outside competence of existing therapeutic expertise in order to minimize the destruction of value within the biotech entity.

6.2 Strategic Recommendations to Small Biotech

There are several considerations that small biotechs have to take into account when deciding on their most effective licensing strategies. When pursuing big licensing deals, a small biotech is always stepping on a fine line between setting itself up to be acquired by the partner, or to cut themselves off from other potential acquirers. Although small biotech is not always in the driving seat to make the decision “to out-license or to get acquired”, it is still possible to make adjustment to its business strategy to increase the probability of either outcome.

- i) If the small biotech does not aspire to become a fully integrated pharmaceutical company and the ultimate exit route is to get acquired, they have to be prudent in not getting encumbered by multiple licensing partners. There has to be at least one product that can act as the hook to get a potential acquirer interested and to create sufficient competitive tension. Formulating a back-end loaded licensing deal would also put pressure upon the pharma to acquire in the future.
- ii) If the investors in the small biotech allow sufficient time and resources for the business to grow in value, out-licensing with multiple partners is integral to allow sustainable growth and it is also the best route to non-dilutive financing. Early out-licensing of the second or third molecule in the product pipeline is practical to get separate validation whilst generating funding and keeping lucrative opportunity for the main molecule intact.

- iii) As a platform technology company, it is difficult to keep the platform novel against radical innovations and the value of the out-licensing deal is also proportionally less than that in product-centric biotechs. Engaging in multiple alliances is also deemed unsustainable as there are often little downstream participation and narrow revenue streams. It is recommended to reposition the business to develop technology that would deliver therapeutic products to become more attractive both as an acquisition target, and to create a more lucrative market valuation.
- iv) For a single-asset biotech, it is advisable to out-license with sufficient competitive tension around the asset in order to be in the position to demand for top-notch deal terms. The most effective deal may still generate decent returns for its shareholders by paying dividends. Otherwise, licensing is advantageous only when it is accomplished with the potential acquirer, since out-licensing the crown jewel without further strategic consideration severely damages the overall valuation of the company.

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Appendix 1: Licensing Deals

Year	Licensor	Licensee	Therapeutic Area	Phase of Development	Bio-Value	Equity	Upfront	Milestone	Royalties
2007	Acambis	Sanofi Pasteur	Vaccine	Phase II	\$80m		\$10m	\$70m	
2007	Acambis	Sanofi Pasteur	Vaccine	Phase III	£20m				
2007	Alizyme Therapeutics	Prometheus Laboratories	Gastrointestinal	Phase II	\$17.5m		\$2.5m	\$15m	
2007	Antisoma	Novartis	Cancer	Phase II	\$890m		\$75m	\$815m	
2007	Argenta Discovery Ltd.	AstraZeneca	Respiratory	Drug discovery	\$500m		\$21m	\$479m	
2007	Ark Therapeutics	Lab21Ltd	Diagnostic	Pre-clinical					5%
2007	Astex Therapeutics	GSK	Drug-metabolising enzymes	Platform Technology	-				
2007	Atlantic Healthcare Ltd	Orphan Australia Pty	Gastrointestinal	Phase III	-				
2007	Cambridge Antibody Technology	iCO Therapeutics	Allergy	Phase I/II	-				
2007	Cambridge Biostability Ltd	Ace Biosciences	Vaccine	Phase I	-				
2007	CeNeS Pharmaceuticals	Ono Pharmaceutical	Anaesthetic	Pre-clinical	-				
2007	Futura Medical plc	SSL International plc	Sexual Health	Phase II	-		£18m		
2007	Isogenica	Wyeth	Unspecified	Drug discovery	-				
2007	Oxford Biomedica	Sanofi-Aventis	Cancer	Phase III	€518m		€29m	€489m	
2007	Plethora Solutions Holdings plc	Sciele Pharma Inc.	Sexual Health	Phase II	-	\$7m			
2007	Protherics plc	Myungmoon Pharma	Anti-inflammatory	Platform Technology	-				
2007	Renovo	Shire	Dermatology	Phase II	\$825m	\$50m	\$75m	\$695m	
2007	Stem Cell Sciences	Merck & Co.	Drug discovery	Platform Technology	-				
2007	Vectura	Undisclosed	Respiratory	-	-				
2006	Acambis	Cambridge Biostability	Vaccine	Phase I	-				
2006	Ark Therapeutics	Sino Tau International	Dermatology	Marketed					
2006	Astex Therapeutics	Pfizer	Drug discovery	Platform Technology	-				
2006	Atugen AG, SR Pharma plc	Merck & Co.	-	-	-				
2006	Biotica Tehcnology Ltd.	Wyeth	Cancer, Immunology	Confidential	\$195m				
2006	BTG	Senexis	CNS	Discovery	-				
2006	Cambridge Biostability Ltd	Panacea Biotec	Vaccine	Platform Technology		£1.935m			
2006	Diabetica	Amylin	Type 2 diabetes	Discovery	\$41m				
2006	Henderson Morley	Cutanea Life Sciences	Dermatology	Platform Technology				\$6.75m	\$115m
2006	Henderson Morley	Amistad Pharma	Dermatology	Platform Technology					10%
2006	Inpharmatica Ltd	Eli Lilly	Drug discovery	Platform Technology	-				
2006	Inpharmatica Ltd	Wyeth	Drug discovery	Platform Technology					
2006	Maelor Pharmaceuticals	Plethora Solutions	Drug Delivery	Platform Technology					
2006	MNL Pharma Ltd.	Avexa Ltd	HIV	Discovery	-				
2006	Morvus Technology Ltd	Nicholas Piramal India Ltd	Diabetes/ Rheumatoid Arthritis	Platform Technology	-				2%
2006	Oxford Biomedica	VIRxSYS Corporation	Gene Delivery	Platform Technology	-				
2006	SR Pharma, Atugen	Pfizer	Age-related Macular Degeneration	Pre-clinical	\$95m		\$2m	\$93m	

Year	Licensor	Licensee	Therapeutic Area	Phase of Development	Bio-Value	Equity	Upfront	Milestone	Royalties
2005	Arakis/ Vectura	Novartis	COPD	Phase II	£200m		£16m	£184m	
2005	Astex Therapeutics	Novartis	Cancer	Pre-clinical	\$520m		\$25m	\$495m	
2005	Astex Therapeutics	AstraZeneca	Cancer	Discovery	£152m		£2.75m	£150m	
2005	Celsis International plc.	BioVentures Inc	Diagnostics	Discovery					
2005	GW Pharmaceuticals	Almirall Prodesfarma	Neurology	Phase III	£46m		£12m	£34m	
2005	Inpharmatica Ltd	Schering AG	Drug discovery	Platform Technology	-				
2005	Inpharmatica Ltd	Mochida	Drug discovery	Platform Technology					
2005	Inpharmatica Ltd	Daiichi Pharmaceutical	Drug discovery	Platform Technology					
2005	Inpharmatica Ltd	Serono	Drug discovery	Platform Technology	-				
2005	ML Laboratories	Maxygen Inc	Drug discovery	Platform Technology	-				
2005	NovaThera	Advanced Bio-Technologies	Dermatology	Discovery	-				
2005	OSI Prosidion	Undisclosed	Diabetes	Discovery	-				
2005	Oxford BioMedica	Undisclosed	Gene delivery system	Platform Technology	-				
2005	Oxford BioMedica	Pfizer	Gene delivery system	Platform Technology	-				
2005	Oxford BioMedica	Biogen Idec	Gene delivery system	Platform Technology	-				
2005	Oxford BioMedica	undisclosed	Gene delivery system	Platform Technology	-				
2005	Oxxon Therapeutics	Xenova Group	Cancer	Phase I	\$83m				
2005	Paradigm Therapeutics	Ortho-McNeil Pharmaceuticals	Neurology	-	-				
2005	PolyTherics	Shabtha Biotechnics	Infectious and inflammatory	Discovery	-				
2005	Procognia	Qiagen	Proteomics	Platform Technology	-				
2005	Protherics plc	AstraZeneca	Anti-sepsis	Phase II	£195m	£7.5m	£16.3m	£171m	20%
2005	Xenova Group plc	PharmaEngine Inc	Cancer	Phase III					
2004	Arachnova Therapeutics Ltd.	Sosei	Stress Urinary incontinence	Phase II	-				
2004	CAT	Wyeth	Drug Discovery	Platform Technology	-				
2004	De Novo Pharmaceuticals	Eli Lilly	Drug Discovery	Platform Technology	-				
2004	Enhance Biotech	ALZA Corporation	Neurology	Discovery	-		\$1.25m		
2004	GE Healthcare	Bristol-Myers Squibb	Drug Discovery	Platform Technology					
2004	GE Healthcare	Regeneron	Drug Discovery	Platform Technology					
2004	Oxford BioMedica	MolMED SpA	Gene Delivery	Platform Technology	-				
2004	Oxford BioMedica	Merck & Co.	Gene Delivery	Platform Technology	-				
2004	Paradigm Therapeutics	Cytomyx Ltd	Drug Discovery	Platform Technology	-				
2004	Vernalis	Endo	Neurology	Marketed	\$145m		\$60m	\$40m	\$255m
2004	Vernalis	Biogen Idec	CNS	Phase II	\$120m	\$6m	\$10m	\$104m	
2004	Xcellsys	Boehringer Ingelheim	Drug Discovery	Platform Technology	-				

Year	Licensor	Licensee	Therapeutic Area	Phase of Development	Bio-Value	Equity	Upfront	Milestone	Royalties
2003	Alizyme	Takeda	Obesity/ diabetes	Phase II	\$42m		\$2m	\$40m	
2003	Antisoma	Roche	Cancer	Phase III	\$500m	\$7m	\$37m	\$456m	10-20%
2003	BTG	Abiogen Pharma	Psychological Disorders	Phase I			£2m		
2003	Cambridge Antibody Technology	Affimed Therapeutics AG	Antibody Technology	Platform Technology	-				
2003	CXR Biosciences Ltd.	Pfizer	Drug Discovery	Platform Technology	-				
2003	Domantis	ImClone Systems	Drug Discovery	Platform Technology	-				
2003	KuDOS Pharmaceuticals	Novacea Inc	Cancer	Phase I	-				
2003	Microsense Biotechnologies	IDEXX Laboratories, Inc.	Food Safety	Platform Technology	-				
2003	ML Laboratories	Antisoma	Drug Discovery	Platform Technology					
2003	Oxford BioMedica	Wyeth	Cancer	Discovery	\$24m				
2003	Phytopharm plc	Yamanouchi Pharmaceutical	CNS	Phase I	\$33m		\$3m	\$30m	
2003	Proteome Sciences plc	IDEXX Laboratories, Inc.	Diagnostics	Platform Technology	-				
2003	Rowett Research Services Ltd	Haptogen Ltd	Drug Discovery	Platform Technology	-				
2002	Active Biotech	Avidex	Autoimmune	Pre-clinical	£5.8m			£5.8m	
2002	BTG	KuDOS Pharmaceuticals	Cancer	Pre-clinical	-				
2002	CeNeS Pharmaceuticals plc	Acorda Therapeutics	Multiple Sclerosis	Pre-clinical	\$13m		\$0.5m	\$12.5m	
2002	Innovata Biomed	Undisclosed	Respiratory		£10m				
2002	KS Biomedix Holdings plc	Nycomed	Cancer	Phase II	\$60m				
2002	KS Biomedix Holdings plc	SoSei Co. Ltd	Cancer	Phase II	\$25m		\$2m	\$23m	
2002	ML Laboratories	Medarex Inc.	Drug Discovery	Platform Technology	-				
2002	Oxford GlycoSciences Plc	GeneProt	Drug Discovery	Platform Technology			\$1m		
2002	Sancell Ltd	ISU Chemical Co Ltd				\$1m			

Appendix 2: M&A Deals

Year	Target Company	Acquirer company	Acquirer Nationality	Value	Public?
2008	CeNeS Pharmaceuticals plc	Paion AG	Germany	£10.9m	Y
2008	Hunter-Fleming	Newron Pharmaceuticals	Italy	€25m	N
2008	Piramed Ltd	Roche Holdings AG	Switzerland	\$175m	N
2007	Cardiff ProTides Ltd	Morvus Technology Ltd.	UK	£5m	N
2007	Acorus Therapeutics Ltd	Maelor plc	UK	£13m	N
2007	Acolyte Biomedica Ltd.	3M	USA	-	N
2007	Alba Bioscience	Quotient BioResearch	UK	-	N
2007	Arrow therapeutics Ltd	AstraZeneca	UK	\$150m	N
2007	Biobest Laboratories Ltd	Integrin Advanced Biosystems	UK	£2.8m	N
2007	Cozart Biosciences Ltd	Concateno	UK	£64.4m	N
2007	CTM Biotech	Alpha Biologics	UK	-	N
2007	DanioLabs Ltd	VasTox	UK	£15m	N
2007	Derms Development Ltd	York Pharma	UK	£17.5m	N
2007	Dextra Laboratories	Summit Plc	UK	£1.5 m	N
2007	Genevac Ltd	Riverlake Partners	USA	-	N
2007	Innovata plc	Vectura plc	UK	\$243m	Y
2007	Molecular SkinCare Ltd	York Pharma	UK	£5.54m	N
2007	Oxxon therapeutics	Oxford Biomedica plc	UK	£16m	N
2007	Paradigm Therapeutics Ltd	Takeda	Japan	-	N
2007	GeneMedix plc	Reliance Life Sciences Private Ltd	India	£14.6m	Y
2007	Rosanto Pharmaceuticals Ltd	York Pharma	UK	£2m	N
2007	Solexa	Illumina	USA	\$600m	Y
2007	Surface Therapeutics	Serentis	UK	-	N
2007	Tripes Discovery Research Ltd	Commonwealth Biotechnologies Inc	USA	\$2.15m	N
2007	British Pharmaceutical Group Forum Bioscience Holdings Ltd.	STADA	Germany	£37.7m	N

Year	Target Company	Acquirer company	Acquirer Nationality	Value	Public?	Premium
2006	Avidex Ltd	MediGene	Germany	€50m	N	
2006	Biotrace International plc	3M	USA	£52	Y	32.70%
2006	Cambridge Antibody Technology plc	AstraZeneca	UK	£702m	Y	67%
2006	Delta Biotechnology Ltd	Novozymes	Denmark	-	N	
2006	Domantis Ltd	GSK	UK	£230m	N	
2006	Equazen Nutraceuticals Ltd	Galencia Group	Switzerland	-	N	
2006	Inpharmatica Ltd	Galapagos	Belgium	€12.5m	N	
2006	NeuroServe Ltd	Lectus Therapeutics Ltd	UK		N	
2006	NeuTec	Novartis	Switzerland	£305m	Y	39%
2006	Pharmagene plc	Asterand	USA	-	Y	
2006	PowderMed Ltd	Pfizer	USA	\$322m	N	
2006	Proteom Ltd.	Amura Ltd.	UK	-	N	
2006	Sciencom Ltd	ReGen Therapeutics	UK	£35,000	N	
2005	Kudos Pharmaceuticals Ltd	AstraZeneca	UK	\$210m	N	
2005	Amedis Pharmaceuticals Ltd	Paradigm	UK	-	N	
2005	Arakis Ltd	Sosei	Japan	£106.5m	N	
2005	Auvation Ltd	EiRx	Ireland	-	N	
2005	Biofocus plc	Galapagos	Belgium	£20.2m	Y	121%
2005	Cambridge Biotechnology Ltd	Biovitrum	Sweden	-	N	
2005	Ionix Pharmaceuticals Ltd	Vernalis plc	UK	£12.5m	N	
2005	Lorantis Ltd	Celldex	USA	-	N	
2005	Microscience Ltd	Emergent BioSolutions	USA	-	N	
2005	Molecular SkinCare Ltd	York Pharma	UK	£5.54m	N	
2005	Tudor Health Care Ltd	Pharmaceutical Development Services	UK	-	N	
2005	XenoSense Ltd	Biacore International	Sweden		N	
2005	Xenova	Celtic Pharma	Bermuda	\$47.5m		
2005	Zeneus Pharma Ltd	Cephalon	USA	\$360m	N	

Year	Target Company	Acquirer company	Acquirer Nationality	Value	Public?	Premium
2004	Aneda Ltd	QbioCom	UK	£1m	N	
2004	Celltech	UCB	Belgium	£1.53bn	Y	28%
2004	Enhance Biotech Inc.	Ardent Pharmaceuticals Inc.	USA	-		
2004	Meridica Ltd	Pfizer	USA	\$125m	N	
2004	Oxoid Ltd	Fisher Scientific	UK	\$330m	N	
2004	Profile Therapeutics	Respironics	USA	£25m	N	
2004	Sterix Ltd	Ipsen	France	-	N	
2003	ArQule (UK) Ltd	Inpharmatica	UK	-	N	
2003	Astex Technology Ltd	metaGen Pharmaceuticals	Germany	£23m	N	
2003	Vernalis plc	British Biotech plc	UK	£48m	Y	11%
2003	KS Biomedix Holdings	Xenova	UK	£8.48m	N	
2003	Merlin Synthesis	Key Organics Ltd	UK	-	N	
2003	Molecular Light Technology Ltd	Gen-Probe	USA	\$11m	N	
2003	Oxford Glycosciences plc	Celltech	UK	£102m	Y	19%
2003	Powderject Pharmaceuticals plc	Chiron	USA	\$878m	Y	4%
2003	Q-One Biotech Group Ltd.	BioReliance Corporation	USA	£42m	N	
2003	RiboTargets	British Biotech	UK	£26m	N	
2003	TheraSci Ltd	CeNeS	UK	£3.7m	N	
2002	De Montfort Biopharma Ltd	Enact Pharma	UK	£0.5m	N	
2002	MedLogic Ltd	Advanced Medical Solutions	UK	£2.5m	N	
2002	Novocastra Labs Ltd	Vision Systems	Australia	\$94m	N	
2002	Physiomics	Intercell	Austria	£7m	N	
2002	QuantaNova Ltd	Biolitec	Germany	-	N	
2002	Xzillion Proteomics	Proteome Sciences plc		£12.6m	N	

Appendix 3: Summary of Key details for the Selected Licensing Case Studies

Year	Licensor	Licensee	Product	Projected Peak Sales	Phase of Development	Bio-Value	Equity	Upfront	Development Milestone	Sales Milestone	Royalty ²²
2007	Antisoma	Novartis	AS 1404	£650 million ²³	Late Phase II	£445m	-	£38m	£190	£162m	Yes
<ul style="list-style-type: none"> • “Antisoma will receive near-term payments of £50 million. £37.5m million was paid immediately and a further £12.5 million when AS1404 enters a phase III trial in lung cancer.” • “An agreement has also been reached that provides Novartis an option to acquire a potential back-up compound to AS1404 that is currently in early-stage development. If this option is exercised, and if this back-up compound achieves development milestones and regulatory approval, Antisoma could receive up to an additional £55 million.” 											
2007	Oxford Biomedica	Sanofi-Aventis	TroVax	£800 million ²⁴	Phase III	£355m	-	£20m	£335m	Nil	Escalating
<ul style="list-style-type: none"> • The Phase III TRIST study of TroVax in renal cancer is co-funded with Sanofi-Aventis. • All other TroVax activities, including development, registration and commercialisation, will be funded by Sanofi-Aventis • “Oxford BioMedica received payments from Sanofi-Aventis totalling £26 million in 2007, comprising an initial payment of £20 million and an early development milestone payment of £6 million. A further milestone payment of £7million was triggered in February 2008 following the third successful interim analysis of the TRIST study by the Data Safety Monitoring Board.” 											

²² Royalty payments are not included in the announced bio-value in these cases

²³ “ING has pencilled in peak annual sales of 1.3 billion USD if AS1404 makes it to the market in lung, prostate, and ovarian settings.” <http://www.forbes.com/markets/feeds/afx/2007/04/19/afx3630421.html>

²⁴ “Peak sales forecasts for TroVax (£800m in 2016) represents approximately 3% of addressable patients and we are comfortable with this number.” <http://www.iii.co.uk/investment/detail/?display=discussion&code=cotn%3AOXB.L&it=le&action=detail&id=3969746>

Year	Licensor	Licensee	Product	Projected Peak Sales	Phase of Development	Bio-Value	Equity	Upfront	Development Milestone	Sales Milestone	Royalty
2007	Renovo	Shire	Juvista	£800 million ²⁵	Late Phase II	£410m	£25m	£37.5m	£87.5m	£262.5m	Escalating
<ul style="list-style-type: none"> • “Shire will make an equity investment in Renovo Group plc of £25 million at a subscription price of £2 per share, which at the date of the announcement represents approximately 7% of Renovo's share capital.” • “On the FDA's acceptance of the filing of the biologics license application for JUVISTA, Shire will pay £12.5 million and on FDA approval, between £25 and £75 million depending on the characteristics of the approved product labeling.” 											
2005	Protherics	Astra-Zeneca	CytoFab	£800million ²⁶	Phase IIb	£195m	£7.5m	£16.3m	£171m	Nil	20%
<ul style="list-style-type: none"> • “The agreement has a potential total deal value, excluding royalties, of approximately £195 million to Protherics, including an initial payment of £16.3 million.” • “AstraZeneca will make a £7.5 million equity investment in Protherics to be paid in cash, at 68.24 pence per share, being a 30 percent premium to the average middle market closing price of Protherics shares over the three months prior to the date of the agreement. AstraZeneca will own approximately 4.3 percent of Protherics’ enlarged share capital.” 											

²⁵ “peak sales ~1.6bn USD per annum.” <http://www.iii.co.uk/investment/detail/?display=discussion&code=cotn%3AOXB.L&it=le&action=detail&id=3969746>

²⁶ “Analysts at Piper Jaffray have estimated that peak sales could be \$1.5bn (£800m), so wholesale revenue might be \$1.2bn.” <http://www.fool.co.uk/news/comment/2006/c060607f.htm>

Appendix 4: Sample Excel Sheets for Valuation Model

Product Attrition Rates

	preclin	Ph I	Ph 2	Ph 3	reg	launch					
% to next stage	38%	100%	40%	100%	54%	100%	100%	45%	100%	82%	100%
% cummul	100%	38%	38%	15%	15%	8%	8%	8%	4%	4%	3.03%
		100%	100%	40%	40%	22%	22%	22%	10%	10%	8%
			100%	40%	40%	22%	22%	22%	10%	10%	8%
			100%	100%	54%	54%	54%	24%	24%	20%	
				100%	54%	54%	54%	24%	24%	20%	
				100%	100%	100%	45%	45%	37%		
					100%	100%	45%	45%	37%		
						100%	45%	45%	37%		
							100%	100%	82%		
								100%	82%		
										100%	

rNPV of Product

Year	0	1	2	3	29	30
Revenues	0.0	0.0	0.0	0.0				160.0	64.0
Marketing	0.0	0.0	0.0	0.0				9.2	8.8
R&D	20.0	40.0	45.0	50.0				0.0	0.0
Total expense	20.0	40.0	45.0	50.0				28.5	9.2
Cashflow	-20.0	-40.0	-45.0	-50.0				150.8	55.2
R- cash flow	-20.0	-21.6	-24.3	-27.0				30.0	11.0
Discount rate	15%								
Cum cashflow	11944.43								
NPV	1092.79								
rNPV	172.96								

rNPV for Licensee (pharma)

Year	0	1	2	3	29	30	
<u>Cash out</u>										
Marketing	0.0	0.0	0.0	0.0				9.2	8.8	
R&D	20.0	40.0	45.0	50.0				0.0	0.0	
Royalties	0.0	0.0	0.0	0.0				30.2	11.0	
Milestones	23.8	40.0	0.0	0.0				0.0	0.0	
Total expenses	43.8	80.0	45.0	50.0				59.6	39.4	
<u>Cash in</u>										
Revenue								160.00	64.00	
Year	0	1	2	3				29	30	
Cash flow	-43.8	-80.0	-45.0	-50.0				120.6	44.2	
yYar	0	1	2	3				29	30	
R- cash flow	-43.8	-43.2	-24.3	-27.0				24.0	8.8	
Discount rate	15%									
Cum cashflow	9316.75									
NPV	741.22									
rNPV	74.94	rNPV	43.33%							share

rNPV for lincensor (biotech)

Year	0	1	2	3	29	30	
<u>Cash in</u>										
Milestones	23.8	40	0	0				0	0	
Royalties	0.0	0.0	0.0	0.0				30.2	11.0	
<u>Cash flow</u>										
Year	0	1	2	3				29	30	
Cash flow	23.8	40.0	0.0	0.0				30.2	11.0	
<u>R- cash flow</u>										
Year	0	1	2	3				29	30	
R- cash flow	23.8	21.6	0.0	0.0				6.0	2.2	
Discount rate	15%									
Cum cashflow	2627.69									
NPV	351.58									
rNPV	98.02	rNPV	56.67%							share

Appendix 5: Interview Questions

Interview Questions for Big Pharmas

Acquisition:

- 1. What are the major problems that you have encountered within the daily operation within the pharma industry?**
- 2. Do you see acquisition of small biotechs as a solution to your previously described problems?**
- 3. In your opinion, what are the major drivers behind acquisitions of smaller biotech companies?**
- 4. What do you look for in the targeted company for acquisition?**
- 5. Would you consider acquiring the company if you could identify a particular product of interest? In your opinions, is acquisition a one-off cost saving activity?**
- 6. What potential drawbacks do you consider that would hinder the decision to acquire?**
- 7. How would you integrate the acquired biotech into your company? Would you consider stripping the asset of the acquired company post M&A, or would you allow more independent development of the acquired company?**

Licensing:

- 1. The number of licensing deals has been rising every year, with an increase of about 2-3 deals per year. What are major drivers do you think has created such an increase in number?**
- 2. There has been a general increase in the bio-value of the licensing deals. In your opinion, do you think that the increasing bio-value of the licensing deals is justified?**

- 3. To what stage does the licensor's product development have to reach before you would consider for licensing? (early stage: cheaper, higher risk, higher ROI; later stage: more developed, looking more into marketing and distribution agreement)**
- 4. What criteria do you use to identify commercially viable early stage innovation? Do you go about approaching the potential licensor?**
- 5. What are the key challenges in identifying early stage innovation?**
- 6. What is the typical revenue split in a licensing alliance/collaboration deal?**
- 7. In your view, what kind of upfront payment, versus milestones, versus royalty rates would you expect for an early / mid / late stage licensing deal?**
- 8. Overall, in long term business development perspective, do you think that it will be cheaper to acquire a company or to license a product?**

Interview Questions for Small Biotechs

Licensing:

- 1. Why would you consider licensing? How does licensing fit into your business model?**
- 2. Which party initiates the licensing process? Was it initiated by the big pharma's interest?**
- 3. Is there a tendency towards out-licensing at an earlier stage of development?**
- 4. At which stage of the product development would you say is the most appropriate time to out-license? Why?**
- 5. Do you feel that you are increasingly having a stronger leverage over negotiating licensing deal terms?**
- 6. In your view, what kind of upfront payment, versus milestones, versus royalty rates would you expect for an early / mid / late stage licensing deal?**
- 7. Do you see licensing to a bigger pharma/ biotech company as an opportunity for future acquisition?**

Acquisition:

- 1. What are major factors that are driving a company's acquisition by a bigger pharma/ biotech entity?**
- 2. What do you look for in your acquirer?**
- 3. What do you see are the pros and cons for acquisition?**
- 4. Do your investors push for acquisition, or would they prefer to continue to build value with the company's growth?**

Interview Questions for VCs

- 1. From your experience, do you reckon there was an increase in the number of M&A deals over the past few years in the UK biotech sector?**
- 2. Nowadays, is there a tendency to fund more later-stage companies rather than early-stage ones? Why is that?**
- 3. Is there a greater pressure to drive earlier exit for the small biotechs? Why is that?**
- 4. Do you think the valuation of UK biotech companies has dropped in recent years? Why?**
- 5. How has the current IPO climate affected your decision upon flotation of the portfolio company?**
- 6. What percentage of return do you expect as a result of a portfolio biotech exit through trade-sale versus an exit through IPO?**
- 7. Would you prefer a trade-sale or IPO for a late-stage portfolio company?**
- 8. What are the main drivers for you to decide to exit through trade-sale of the portfolio company?**
- 9. Do you view licensing opportunity as a potential lead-on for future acquisition?**