We all rely upon medical and scientific advances; however, because of the risks intrinsic to research and development, the associated funding is inherently risky as well. How does the bio-pharma industry operate and how has the industry been affected by the financial crisis? The UK government provides significant financial support to the bio-pharma sector in the form of research and development tax credits and is again targeting the pharmaceutical industry as a key driver of UK economic prosperity. The coalition government has recently issued a consultation document “patent box” where the objective is to provide financial incentives to develop and exploit bio-pharma intellectual property in the UK.

This study investigates the UK SME bio-pharma sector. It tracks AIM listed bio-pharmas to investigate return on investment and the level of capital at risk, considers the impact of the financial crisis on the sector, and seeks the views of senior executives of private and publicly quoted bio-pharmas and industry representatives. The study concludes by presenting the case for innovative short and medium term government-led policy initiatives for the sector and highlights four central areas in which the current bio-pharma business model could evolve.

EAN 9781904574798

Price: £10.00
UK bio-pharma: Innovation, re-invention and capital at risk

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Published by

The Institute of Chartered Accountants of Scotland
CA House, 21 Haymarket Yards
Edinburgh EH12 5BH
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Foreword

We all rely upon medical and scientific advances; however, because of the risks intrinsic to research and development, the associated funding is inherently risky as well. Unfortunately, it seems that these risks increase as economic circumstances deteriorate. So how does the bio-pharma industry operate and how has the industry been affected by the financial crisis? The government – recognising the importance of this sector to the UK economy – recently issued a consultation document entitled 'patent box', the objective being to encourage companies to develop and exploit their intellectual property in the UK.

This study investigates the UK SME bio-pharma sector. It tracks AIM listed bio-pharmas to investigate return on investment and the level of capital at risk, considers the impact of the financial crisis on the sector, and seeks the views of senior executives of private and publicly quoted bio-pharmas and industry representatives. The study concludes by presenting the case for innovative short and medium term government-led policy initiatives for the sector and highlights four central areas in which the current bio-pharma business model could evolve.

This project was funded by the Scottish Accountancy Trust for Education and Research (SATER – see page 57). The Research Committee of The Institute of Chartered Accountants of Scotland (ICAS) has also been happy to support this project. The Committee recognises that the views expressed do not necessarily represent those of ICAS itself, but hopes that the project will add to the debate about the future of UK bio-pharma.

Allister Wilson
Convener of Research Committee
July 2011
Acknowledgements

In order to complete our research work we have obtained the support of a number of senior executives in private and publicly quoted SME bio-pharma companies and also industry experts in big-pharma. We would like to thank this group for giving up their time to be interviewed for this research project. We would also like to thank Dr Peter Fellner, Non-Executive Chairman of the Board of Vernalis PLC, for his help at the start of this project and the anonymous reviewers for their helpful and constructive comments.

Finally, the Research Committee and the researchers are grateful for the financial support of the Scottish Accountancy Trust for Education and Research, without which the research would not have been possible.
Executive summary

Background

Small and medium enterprise (SME) bio-pharmas play a significant role in the development of a knowledge-based competitive economy because they act as an incubator of creativity for the development of pharma-based products which they steer towards regulatory approval. Their contribution is predominantly the development of new pharmaceutical products which can then be licensed or sold on to big-pharma.

The business model governing SME bio-pharma is, however, a delicate balancing act between, on the one hand, progressing product along its development pipeline, and on the other, securing sufficient cash resources to finance this product development. As new products are conceived and then progress into their subsequent phases of clinical testing and final approval, the identity of equity investors’ changes from initial business angel or venture capital partnership, into possible institutional or big-pharma investors. It is a business model where investors are looking to try and ‘hand-on’ ownership and realise a return on their investment and so milestone reports about pipeline progress take on added significance because these influence analysts’ opinions and market valuations.

The SME bio-pharma business model is complex because it is subtended within a multifaceted network of stakeholders including: universities, medical research centres, charities, national and regional government, regulatory bodies and agencies, big-pharma, business angels, venture capital and other institutional investors. Individual SME bio-pharma firms located within this business model are thus challenged by the variable circumstances, demands and interests of these stakeholders.

This report reveals how the financial crisis and its aftermath have modified investor and management behaviour within the bio-pharma business model.
Research objective and method

The research objective of this report has been to discover the extent to which the knowledge based UK SME bio-pharma business model is robust or fragile in the aftermath of the recent financial crisis. The investigative method employed in this report combines numbers and narratives. The analytical framework extracts financial data reported by the London Stock Exchange Alternative Investment Market (AIM) for SME bio-pharmas and uses this information to construct unique datasets. These datasets track total equity investment and market value returns for all AIM listed SME bio-pharmas to establish the extent to which capital is at risk in this business model. In addition financial data has been extracted from company financial report and accounts to demonstrate how many AIM listed SME bio-pharma’s burn cash and the extent of their cash reserves. Narratives have been collected from semi-structured interviews with senior executives and six company cases, representing a broad range of therapeutic research areas, age profile, growth strategies and type of ownership, are employed to explore the challenges to sustaining viability.

Key findings

Investors are coming back into the market but they are generally investing in products in a later stage of clinical testing because these products have passed initial screening tests and so they promise a more secure financial return.

Analysis in this report of bio-pharmas that have listed on the Alternative Investment Market (AIM) reveals that they have generated strong returns on investment. Only a small proportion of capital invested in AIM listed bio-pharma would seem to be ‘at risk’. This should positively encourage investors and those wishing to list a bio-pharma SME on AIM.

Managers have significantly cut back on development expenditures, putting projects on hold, reducing the volume of product in pipeline and selling off assets to secure cash funding. Interviews carried out with senior executives in both quoted and private SME bio-pharmas reveal how the financial crisis has modified their behaviour. Senior executives
have struggled in recent years to ‘keep it all going’ in circumstances where cash funding, in some cases, almost dried up or follow-on funding to the extent requested was not forthcoming to meet business plans.

It is difficult to persuade equity investors to put in more cash when not only is the equity base diluting, but market valuations are also on a downward trajectory. Analysis of the most recent interim reports of AIM listed bio-pharmas revealed that two-thirds were burning cash and that of this group roughly 60% had less than 6 months of cash in reserve.

The recent turnaround in capital market valuations is necessary but it is not a sufficient condition for sustaining the SME bio-pharma knowledge-based business model.

**Policy implications**

This report argues for imaginative policy interventions in the short-run and medium-term. These should be directed at sustaining the complex stakeholder network that make up the bio-pharma knowledge-based business model.

In the short-run, we argue that Government funding must continue to sustain early stage research and product development in universities and medical research centres.

Cuts to university and medical research institute funding will limit the UK’s capacity to develop new pharma molecules for diagnostic testing and patient therapies. The flow of spin-outs from universities and medical research centres, if restricted, will undermine opportunity for investment and growth.

We also believe that there is a strong case for government emergency funding which can be deployed quickly to prevent disorderly downsizing. This report reveals that the complex knowledge-based stakeholder network within which SME bio-pharmas operate is fragile and when financially distressed, the intangible asset base either corrodes or is lost.

In the medium term the question to be answered is how can the business model be adapted to accommodate the lower risk appetite from investors that is starving early-stage research funds?

According to a senior vice president of a major bio-pharma the response to the question is one which must:
Re-draw the way in which the bio-pharma business model is financially supported and how risk and return is distributed between the different stakeholders involved in a complex development network — working back from patient neurology into the university/medical research lab.
(Company 2: Vice President)

Elements of the evolution of the bio-pharma business model could include:

- Access to NHS clinical datasets to provide a significant knowledge resource to strategically drive UK drug discovery.
- Government funding to UK universities and medical research institutes balancing academic standards with a sense of commercial urgency.
- Open innovation investment consortia to spread financial risk that is inherent in long complex development and testing value chains.
- Strengthened regional network agencies to provide advisory, mentoring and support services into the stakeholder network supporting the bio-pharma development chain.

Adapting the SME bio-pharma business model for a sustainable future will be a challenge. Innovative policy interventions, clever regulatory arrangements and imaginative funding mechanisms are required. The purpose is to secure bio-pharma’s contribution to UK national output, employment and balance of trade.
1. Background

The SME bio-pharma industry has flourished in recent years, encouraged by government financial incentives and the changed strategic priorities of big-pharma companies. Universities and medical research centres have been encouraged to commercialise their bio-pharma knowledge-based intellectual assets into spin outs with funding from business angels and venture capitalists.

Big-pharma’s business model has also changed. Major pharmaceutical firms are looking to undertake less research and development (R&D) in-house and out-source to SME bio-pharmas where the latter undertake initial development and some clinical testing of a new product.

Encouraged by supportive government policy, tax concessions, financial incentives and the outsourcing strategies of big-pharma, the number of SME bio-pharmas listed on the Alternative Investment Market (AIM) increased significantly during the last decade peaking at 76 in 2007 with a market value of £3.5 billion.

For investors in both listed and privately owned SME bio-pharmas, there is the possibility of generating substantial market value return on invested capital if development and testing result in favourable clinical assessments about products that are in the pipeline.

To maintain their product development and clinical testing pipelines, SME bio-pharmas need to maintain a flow of equity follow-on funding and so they regularly need to go back to existing or new equity investors for additional cash.

Equity investors providing this follow-on funding are, in turn, generally looking for SME bio-pharma managers to deliver pipeline progress towards regulatory approval. This reduces the risk of invested equity capital because share prices and market value return on investment multiples are positive and on an upwards trajectory.

The SME bio-pharma business model is complex because it depends on sustaining product development, delivering positive milestone reports and encouraging investors with variable motivations to provide funding to support product development.
The recent financial crisis and its aftermath threaten to undermine the knowledge-based UK bio-pharma business model. This report investigates the extent to which innovation, re-invention and capital are at risk.
2. Research approach

The research approach taken in this report combines both numbers (analysis) with narratives (interviews). It is a research approach utilised by Froud et al. (2006) and more recently by Gleadle and Haslam (2010) and by Andersson et al. (2010).

The first section of this report focuses on SME bio-pharmas that have listed on AIM. The current research project has involved constructing a unique dataset to track all AIM listed firms and bio-pharmas, covering Initial Public Offering (IPO), follow on funding and market value on a monthly basis from 1998 to June 2010. This report tracks AIM listed bio-pharmas entering and exiting and their IPOs and follow-on funding relative to their market value added. It also compares the bio-pharma group of firms relative to the average AIM listed company. The objective is to consider the extent to which AIM listed bio-pharmas have delivered a strong return on invested funds or to judge whether they represent significant capital at risk.

This is followed by a consideration of the impact of the financial crisis and its aftermath on the SME bio-pharma business model in terms of the supply of follow on funding and firm finances. To what extent do firms have the ability to cut back on expenditure levels and how much cash burn do they have in reserve? Using financial information extracted from annual report and accounts, we reveal the extent to which AIM listed firms are cutting back on their development expense as they struggle to maintain reasonable cash reserves.

The next section of this report summarises some of the key ‘narratives’ collected from a series of semi-structured interviews with senior executives managing private and publicly quoted SME bio-pharmas and other representatives of the industry. Interviewees gave their formal consent to be interviewed in return for their anonymity. The interviews were taped where possible, transcribed, and analysed. Details of these interviews are shown in table 1.

The final section consists of a series of company mini case studies, the purpose of which is to reveal the different challenges faced by SME firms operating in the bio-pharma sector. These cases reveal a complex set of interrelated challenges that revolve around financial market conditions.
and the struggle to maintain and prioritise product development. Six company cases are chosen from Table 1 because they represent a broad range of therapeutic research areas, age profile, growth strategies and ownership (private and publicly owned).

**Table 1  Interviewees and their company profile**

<table>
<thead>
<tr>
<th>Company</th>
<th>Activity</th>
<th>Listed/private</th>
<th>Interviewees and position in company</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SME specialist big pharma supplier.</td>
<td>Toronto stock exchange.</td>
<td>CFO.</td>
</tr>
<tr>
<td>2</td>
<td>Large cap big pharma.</td>
<td>US NASDAQ.</td>
<td>Senior Vice President &amp; Head of Worldwide Development.</td>
</tr>
<tr>
<td>3</td>
<td>Big four accountancy firm.</td>
<td>Not applicable.</td>
<td>Director Transaction Advisory Services AIM bio-pharma.</td>
</tr>
<tr>
<td>4</td>
<td>SME cancer vaccines and gene therapy.</td>
<td>AIM then London main stock exchange (LSE).</td>
<td>CEO, CFO and Chief Scientific Officer (CSO).</td>
</tr>
<tr>
<td>5</td>
<td>SME metabolic disease, neuro-degeneration.</td>
<td>London main stock exchange (LSE).</td>
<td>Acting CEO, COO (Chief Operating Officer)/Rescue Consultant and Finance Manager.</td>
</tr>
<tr>
<td>6</td>
<td>SME central nervous system (CNS) and oncology.</td>
<td>London main stock exchange (LSE).</td>
<td>Chairman.</td>
</tr>
<tr>
<td>7</td>
<td>SME small-molecule protein-coupled receptors (GPCRs).</td>
<td>Private company.</td>
<td>CEO.</td>
</tr>
<tr>
<td>8</td>
<td>SME human cancers.</td>
<td>US NASDAQ.</td>
<td>Executive VP/COO.</td>
</tr>
<tr>
<td>9</td>
<td>SME fragment-based drug discovery.</td>
<td>Private company.</td>
<td>CEO/CSO, CFO &amp; Chief Business Officer.</td>
</tr>
<tr>
<td>10</td>
<td>SME central nervous system and oncology.</td>
<td>Listed on AIM.</td>
<td>CFO and Head of Research &amp; Development.</td>
</tr>
<tr>
<td>11</td>
<td>SME protein drugs, vaccines and anti-cancer drugs.</td>
<td>Listed on AIM.</td>
<td>CEO and CFO.</td>
</tr>
</tbody>
</table>
3. Research findings

SME bio-pharma firms operate within a complex business model (see Fig.1). On the one hand, products being developed pass through various stages: concept, clinical testing and final regulatory approval. Meanwhile as products are developed, regular milestone reports are issued to inform current and potential investors (and other stakeholders) about progress towards approval.

The average firm will have a product portfolio where a number of products are at various stages of development and testing. Some, but not all of these products, may generate favourable milestone reports. Often products are ‘reinvented’, that is, repositioned into complementary or alternative therapeutic development channels.

Milestone reports matter because they reveal the extent to which innovative or reinvented product in the pipeline is progressing towards regulatory approval. Positive milestone reports encourage analysts to boost share prices and therefore also motivate investors to provide much needed follow-on equity funding. Firms that progress product development move along a funding escalator because larger scale clinical testing is also more expensive.

As product progresses from development into clinical testing and final approval, the identity and motivations of equity investors change. Original investors might include: universities, charities, business angels and venture capital partners. A successful IPO and listing on the stock market, for example on the AIM, provides a possible exit route for existing investors. It can also attract new investors: investment banks, hedge funds, private equity investors and big-pharma partnerships. Securing a big-pharma partnership agreement not only underwrites additional equity funding, but also helps to raise a firm’s profile, often boosting quoted market value and making it easier to leverage additional financial resource.
It is generally accepted that capital is at risk in the bio-pharma business model because of the gap between ‘financial tolerance’ and ‘development time horizon’. However, investors managing a portfolio containing all AIM listed bio-pharmas would have generated a strong return on investment over the period 1998 to 2010. This report distinguishes between capital investment at risk and the challenge in the aftermath of the financial crisis to sustain complex stakeholder networks that make up the bio-pharma business model.

**AIM listed bio-pharma**

In December 1998 there were just six bio-pharma firms listed on London’s AIM. By 2007 this number had reached a peak of 76 firms but as of June 2010 there were just 41 firms. This reduction of 46% compares to a 27% reduction in firms listed across the AIM as a whole. This report’s analysis focuses bio-pharma firms listing, exiting and surviving on AIM during the period December 1998 to June 2010 (Chart 1).
Over the period 1998 to December 2007, a growing number of bio-pharmas are actively listed on AIM, but thereafter the number of firms falls from its peak to just over forty by June 2010 (Chart 1). In total 106 bio-pharmas listed on the AIM during 1998 to June 2010, of which 65 had exited and 41 were still listed as at the end of June 2010. There are also two distinct periods: 1998-2007 where more firms are entering than exiting and 2008 to 2010 where more firms are exiting than entering (Chart 2).
In this report the analysis focuses both on ‘survivors’, that is those firms still listed on the AIM as at the end of June 2010, and those ‘exiting’ i.e. de-listing from AIM before 30th June 2010. The ‘exiting’ firms are split into two groups: ‘strong exits’ which leave the AIM with a strong market value for investors and those which generate little or no market value on exit: ‘weak exits’.

In an earlier period (2000-2005) the average market value of a bio-pharma listed on AIM exceeded that of the average AIM listed firm (Chart 3). Thereafter, this reverses and by 2010 the average AIM listed firm has a market value of £50 million and the average bio-pharma roughly £40 million.

Source: London Stock Exchange AIM
http://www.londonstockexchange.com/companies-and-advisors/aim/aim/aim.htm
Strong market valuations matter for bio-pharmas because firms are competing for equity funds from existing or potential new investors. In normal circumstances where firms are generating operating profit or surplus cash, they will seek to justify their need for additional external funding with projections about future growth and their ability to service and pay back invested funds. In the bio-pharma business model narratives about pipeline progress act as a substitute for ‘sensible’ financial numbers.

The SME bio-pharma business model can be characterised as one of ‘cash burn’ because, in general, equity finance is employed to cover the expense of research, development and clinical testing. Typically the average AIM listed bio-pharma firm burns cash because expenses generally exceed income from milestone payments and license fees (Chart 4).
In 2007 the average AIM listed bio-pharma’s operating expenses exceeded income by 41%. More recently, with the onset of the financial crisis, a scarcity of equity funding has forced UK bio-pharma chief executives to cut costs (product development schedules and the range of products in pipeline) in order to limit cash burn. Conserving cash resources is now a primary business objective for most AIM listed bio-pharmas because over 70% of companies operate under a ‘cash burn’ regime (Chart 5).
If we focus on the firms listed on AIM at the start of 2010, analysis of the most recent interim reports for this group of bio-pharmas reveals that 73% were burning cash reserves. Of this group of firms, 54% were operating with less than six months of cash reserves and 75% with between zero to 12 months’ cash in reserve. This means that one third of bio-pharmas listed on the AIM as at the start of 2010 had less than six months of cash resource to cover operating expenses (Chart 6).
Maintaining the flow of funds after the IPO with subsequent follow-on funding is thus critical. The recent financial crisis has reduced both the level and frequency of IPO and follow-on funding, so threatening the bio-pharma business model because equity funding acts as the oil in the machine that keeps it all going (Chart 7).

Chart 7  **AIM-listed bio-pharmas total investment (monthly IPO and refinancing £ m)**

Source: London Stock Exchange AIM
http://www.londonstockexchange.com/companies-and-advisors/aim/aim/aim.htm

Equity investors are not in a marathon, but instead, they are engaged in a relay race, trying to hand on the ownership baton because this offers the opportunity to exit and realise a market value return on total investment. For AIM listed ‘survivors’ and ‘exiting’ firms it is possible to track IPO and follow-on funding and contrast this total investment with market valuations to reveal a return on investment. The analysis starts by considering the companies included in the ‘survivor’ group of bio-pharmas that are listed as at June 2010 (Chart 8) before turning to consider the return on investment from exiting companies.
In the heady days when bio-pharmas first started to list on AIM, the market value to total investment (IPO plus refinancing) ratio hovered around 7:1 but the ratio has since progressively narrowed (Chart 9) and is now standing at roughly 2.5:1. However, there have been periods when the gap between market value and total investment narrows. For example, between 2007 and late 2008 this gap narrowed from roughly £1 billion to £0.15 billion (Chart 8). Over the whole period the bio-pharma market value to investment ratio is higher (3.5) than that of the average AIM listed firm (2.9).

Source: London Stock Exchange AIM
http://www.londonstockexchange.com/companies-and-advisors/aim/aim/aim.htm
Turning to the performance of the 65 exiting companies which attracted £1.3 billion of total investment (IPO plus follow-on funding), this group can be split into two. Firstly, there are the ‘strong’ exits where there is a strong market value on exit and secondly, the ‘weak’ exits where there is little or no market value recorded at the time of exit (see Table 2).

**Table 2  AIM bio-pharmas: Total investment and market value return 1998 to 2010**

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>Strong exits</th>
<th>Weak exits</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPO + Equity financing £bn</td>
<td>0.7</td>
<td>1.1</td>
<td>0.20</td>
</tr>
<tr>
<td>Market value £bn</td>
<td>1.7</td>
<td>3.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Market value to investment ratio</td>
<td>2.5</td>
<td>3.0</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Source: London Stock Exchange AIM. All values at as end June 2010
http://www.londonstockexchange.com/companies-and-advisors/aim/aim/aim.htm
An average investor holding a full portfolio of AIM listed bio-pharmas and participating in all equity follow-on funding opportunities would have experienced both ‘strong’ and ‘weak’ returns on investment at final exit. Significantly, it is found that weak exiting firms accounted for a relatively small fraction (11%) of total investment made into an AIM listed bio-pharma portfolio (Chart 10). Roughly half (55% or £1.1 billion) of our ‘average’ investor’s funds would have been placed in strong exiting firms and generated a market value return of £3.3 billion, a market value to investment ratio of 3:1. The remainder of their investment (34%) would still be in survivor firms listed on AIM where a final exit is still to be made. As at the end of June 2010, a total equity investment of £0.7 billion in this group of firms had a market value of £1.7 billion, representing a return on investment of 2.5:1.

*Chart 10  AIM bio-pharma total investment in strong, weak and surviving firms*

The bio-pharma business model is highly dependent upon refinancing because firms consume externally sourced cash resources in
order to advance product development in their pipelines. In the recent financial crisis many firms have been, and still are, close to running out of cash and so are freezing product development and/or rationalising products in pipeline.

Analysis reveals an important distinction between the ‘risk’ attached to sustaining a complex bio-pharma stakeholder network, which is relatively high, and risk connected with return on capital which is relatively low. The recent upturn in market valuations running into 2011 will bring much needed respite, encouraging equity investors to provide additional funding. In turn this will increase the flow of product development, the frequency of milestone reports, the level of partnership deals, licensing agreements and ownership trades, so strengthening the stakeholder network that binds together this business model.

Bio-pharma: narratives and practitioner perspectives

For this report a series of interviews was carried out with senior executives involved in bio-pharmas. The interviews revealed a commitment to innovation, re-invention and creativity. However, the structure and organisation of the bio-pharma business model needs to change. Although innovation and creativity drive this business model, a shortage of financial resource was acting to put a brake on momentum so that firms increasingly struggled to keep it all going.

Bio-pharma senior executives pay a great deal of attention to generating encouraging milestone reports. In the absence of ‘sensible’ financial information, the narratives of the milestone report take on added significance in helping to secure further tranches of funding, either as follow-on equity finance or as stage payments from partnership agreements. There is an implicit tension here that becomes explicit when capital market conditions deteriorate because lower market valuations reduce the incentive to provide follow-on funding, making it much more difficult to maintain product development.

Executives interviewed revealed the pressure they have been under in recent years to cut back costs, either by reducing product in pipeline, slowing down progress or both. This led many of those interviewed to
question the viability of the current business model and to offer some insights into how this may need to change in order to secure a sustainable future. One of the interviewees observes:

_The object is to reconsider the way in which finance, government, universities and companies [the institutions involved] in development of bio-pharma knowledge re-draw the form of business model, and how risk and return are distributed to the different players involved in a complex development chain – working back from the patient neurology into the research lab._ (Company 2: Vice President)

**Innovate**

The interviews revealed a strong commitment to innovation and creativity but this was always tempered by a sense of commercial realism. This juxtaposition exposes the tension between discovery and commerciality. In big-pharma, interviewees focused on the fact that R&D spend made up an increasing share of sales revenue but was not as productive as it once had been:

_These guys are just coming back to the same point that they realise that discovery isn’t delivering in a large organisation and, you know, speculate as to what the specific reasons are, that’s simply the case and therefore they’re pulling back._ (Company 8: CEO)

A big-pharma senior executive recognises the symptoms of their development deficit but, as yet, there is considerable reluctance to restructure into an openly innovative system:

_The challenge that is banded about now is ‘Open Innovation’. So one of the questions we have to address is “Where is the real competitive know-how of the company and what should be shared for the common good?”. And, I think that’s a big discussion and I think that’s one point and I think that there has been protectionism within companies and_
frankly I question how innovative companies really are. (Company 2: Vice President)

The inflexibility of big-pharma is captured by the thoughts of an SME CEO who had left such a multinational company:

In 1999 I was at the big-pharma company... more in a kind of technology part of the organisation. And to cut a long story short, I had kind of felt that there was some specific ideas or issues which should be addressed within the space of early drug discovery which I thought would be better addressed by building a new approach to those candidates. So without going into too much detail, I felt that actually the best thing to do would be to completely leave everything I had here and just resign and set up a company to do this. (Company 8: CEO)

Big-pharma’s strategy has been to out-source product development, taking equity stakes or paying licence fees through partnership agreements with SME bio-pharmas that have promising product in pipeline. For SME bio-pharma, such deals are not just about knowledge and innovation, but also about funding to sustain knowledge development activity:

Talking about how to create knowledge – you need money to do that – and that’s part of the oxygen supply. (Company 2: Vice President)

However, according to one SME CEO, a persistent problem remains that capital markets only value late-stage clinical assets and so will not recognise a technology on its merits. big-pharma too are interested only in later stage clinical development such that SME bio-pharma have to invest much more heavily than was previously the case, before big-pharma will come on board. To quote the Chief Scientific Officer (CSO) of one SME bio-pharma:

So, we’re sort of dancing around the handbags in a disco, really, and meanwhile we’re all running out of cash. (Company 7: CSO)
For SME bio-pharma senior executives the pressure is both to create knowledge-based product and also to sustain equity funding. These pressures force firms to re-invent and re-position compounds/products into new market segments less exposed to direct intense competition.

**Re-invent**

Re-inventing often involves managing the expectations of original equity investors as new ideas are championed:

*A lot of our shareholders came into share ownership... because they believed the obesity story. And we've got a long tail of shareholders who've come in for a reason and we're now no longer championing those ideas. So we need to manage those expectations and we need to manage some returns as part of that process.* (Company 5: Acting CEO)

*About a year ago we were just about to ‘crash and burn’ with a Phase III programme – very risky programme in the area of neuro-regeneration Huntington’s. The company was almost out of money and had to re-think what it did. We had to reposition the compound and raise additional funds roughly $100 million. This compound has the potential for revenues of several billion in cardiovascular, [and] it is now fit for purpose and it is now better funded obviously and has a better set of overheads.* (Company 2: Vice President)

**Re-position**

SME bio-pharma executives also talk about the need to reposition their firms:

*Yes. Well, I think we’ve had a focus in the last 14 months here. And I think, you know, the challenge in the past was trying to pursue both the functional foods and the pharmaceutical program with a small team and limited resources. And there was the, you know, the balancing and trying to get the functional food to finance the pharmaceutical [program], which was a tough balancing act... my approach is*
always to look at the balance sheet and look at well, actually what are the assets that we can progress... and what is a critical path to a liquidity event? And then to really focus on that critical path with some selfishness and not doing some of the regular day to day things that you would normally do, because when you’re in a sort of, a turnaround situation you do need to say ‘What are the key things that are really going to make a difference?’ and make sure you do those really well. (Company 5: Rescue Consultant)

Milestone reports supporting liquidity events

Milestone reports are ‘in our DNA’. (Company 4: CEO)

These reports convey to investors the progress of specific products in pipeline and the extent which they are progressing along phases of development and clinical testing. Milestone reports are significant in the absence of ‘sensible’ financial information. The milestone report highlights the tension between on the one hand, the motivations of SME bio-pharmas to develop innovative product and on the other hand, the calculations of investors:

...we did have a battle with our potential funders going through the fact that there were very little milestone announcements coming out of the trial. And it also throws up the challenge between those who want to invest for a longer term, and [those interested in the shorter term] because what they [the shorter-term investors] were interested in was getting in, if there was some good news, getting out. (Company 5: COO)

Managers interviewed revealed the pressures they are under to keep equity investors informed, especially when many of those investing are looking for good news to boost share prices and so facilitate an exit possibility:
The equity market needs to know that the investment it has made is doing something, and that there are prospects for the future, and we’re under a lot of pressure to keep making announcements, keep reminding people that we’re out there and making progress. Those who are most vociferous in asking for that information tend not to be the big savvy professional investors but, to a large degree, are smaller retail investors who are... I don’t know, maybe their motivation is short-term and that they’re hoping that we’ll announce a piece of news, there will be a spike in the price and that would give them an opportunity... to get out. (Company 4: CFO)

The interviews revealed the mix of investor types and how their reactions to milestone reports cut both ways:

We have a nucleus of loyal and committed shareholders. We also have experienced several secondary issues, that quite often we will issue new stock in a secondary issue, usually at a discount to the prevailing price, and some of it will go to our long-term supportive shareholders, and some of it will go to new people who we’ll see on the share register for six months or so and then [we] find that they have churned that stock out and moved onto something else. So, there is a real division. (Company 4: CFO)

Milestone reports represent an important inflection point at which information is shared with equity investors. Often a strong milestone report will help to boost share prices and make it easier to generate follow-on funding:

In order to raise the £21m last year, the firm had made excellent progress scientifically, meeting/exceeding the milestones in the seed funding such that the technology could run on an industrial timescale. Investors could see that the impact of the technology was very large. (Company 7: CEO)
Milestone reports also play a significant role in the managed relationship between SME bio-pharma and big-pharma where partnership contracts have been exchanged:

*Again the R&D that we would do is driven by them [big-pharma] in the sense that they give us a specific employ that they want and in negotiating our service contract with them, we would devise a development plan which would be costed based on the number of staff, the grade, their charge-out rate, our overhead recovery rate and we would do that on a specified project plan where there would be measurable achievement points and obviously there would be regular interaction and if we hit certain milestones, that triggers the section of the next stage of the contract. (Company 1: CFO)*

However, this bio-pharma CFO goes on to comment how risky the whole R&D stakeholder process is:

*This is R&D, it’s not like us building a house, you know, and saying we want stage payments when we’ve got the walls up. You might put the walls up and find actually the walls won’t stand up. So there’s no guarantee for us that we’ll move from one stage to the next. There’s definitely a risk involved and you know we take risks ourselves in developing our own products so we have to balance this risk within our portfolio. (Company 1: CFO)*

SME bio-pharma milestone reports assume great significance in the absence of ‘sensible’ financial information. All of those interviewed stressed the critical importance of reporting progress in a timely fashion. The CEO (Company 4) observes:

*You should be making announcements at significant project milestones, rather than drip-feeding information and putting [out] small amounts of data which could be taken out of context. So, there are tensions between saving data up until you’ve got a lot of it and it’s robust, and the very real tension that people want to know what’s
However, the continuing pressure for news flow has very real effects on bio-pharma firms’ behaviour. One SME bio-pharma executive comments how the firm should be ensuring that its production capacity is adequate. Unfortunately, building such capacity is not regarded as newsworthy in comparison to pipeline development with the result that the pressures often force firms to prioritise the latter so as to reach rapid endpoints.

A favourable milestone report is significant not only because it can help to boost share prices but also because it increases investor confidence and the probability that the next “liquidity event” will be a success.

Bio-pharma: funding environment

Bio-pharma SMEs seek funding from a variety of sources: European and national governments, universities, NHS bodies, charities, private equity and venture capital partners, equity investors (retail and institutional) and big-pharma partnerships to name but a few.

The funding environment for SME bio-pharma has not been immune from the effects of the recent financial crisis. In fact, two of the main sources of funding for SME bio-pharma have been so affected. For example, companies listed on AIM have seen the total value of IPO and follow-on funding peaking in 2006 at £450 million and falling well below £100 million as at 30th June 2010 (Chart 11). Private equity and venture capital finance for the bio-pharma sector is also down 55% on its peak (BVCA, 2009).
Source: London Stock Exchange AIM. All values at as end June 2010
http://www.londonstockexchange.com/companies-and-advisors/aim/aim/aim.htm

The interviewees revealed their frustration with both the complexity of funding within this sector and the challenges that they face in maintaining sufficient cash resources to maintain product development:

*These days there are no rules about getting funding, only problems, and it is more difficult to get investors than was the case 10 years ago.*
(Company 7: CEO)

This same bio-pharma CEO goes on to comment:

*The waters are not warm... There is a persistent obsession of the market with companies that have not done well such as British Biotech as long as 10 years ago. The City is risk averse so that flotation is very tough.*
Moreover, according to one bio-pharma executive, venture capital, traditionally a significant funder for UK life sciences has ‘basically fallen out of bed’ as venture capitalists turn their attention primarily to the US where, unlike the UK, there have been a number of significant bio-pharma success stories.

With regard to EU funding, there is frustration with the process and timing:

_We’ve got an EU grant application that went in in November 2009. If we’re successful, it will probably be early 2011 before we actually culminate the project. Because the amount of time it takes… because even once you’re successful you’ve then got a six to nine month negotiation process with the EU. And it’s all those timescales that just don’t work._ (Company 5: COO)

There is also criticism of national government for delay and indecision:

_They’ve been promising funding for biotech now… there was a speech from Mandelson seven months ago and nobody knows what the hell is going on with that still. Lord Drayson’s still very active in getting money as well. But nothing ever happens so it makes you loathe to think anything can happen from that direction. About the only thing you can get is an R&D tax credit which actually we get and is of benefit to us._ (Company 4: CEO)

The problem of securing funding for bio-pharma has forced some UK firms to list on the NASDAQ where fundraising is viewed as easier, partly because there are more specialist funds. However, to quote the CEO of one such company:

_What we don’t have is we don’t have an adequate capital base in order to develop the products that we do have, so again, there’s a very strong symbiotic relationship between our ability to generate new cash, either by licence milestones or by capital raises, and our ability_
to promote one of our internal candidates, of which we have a number.
(Company 8: Executive VP)

Other parts of the funding model are also under stress. Those interviewed suggested that universities’ spin-outs are trying to extract immediate gains but are failing to set up viable financing models. Moreover, government funding is not specifically targeted at bio-pharmas:

Some of the blame for the lack of funding, actually rests with some of the universities who were trying to capitalise on the IP [intellectual property] they had in spinning off companies, which were then able to generate one or two years’ worth of money which wasn’t sufficient to take it to the point where it had value to raise more money.

And I think that we’re where the least grant funding is available [i.e. for bio-pharmas themselves]. The majority of it tends to be aimed either within the NHS or within the academic community. And I’m thinking in particular of the Technology Strategy Board. And even the small amount that is available for the more commercial organisations, again, the application process, and the time it takes before you get a decision, is too long. (Company 5: COO)

SME bio-pharma depends to a large extent on equity investors and big-pharma for funding. However, some of those interviewed question the reliability of these sources of finance:

I think that the... key dynamic for the business model, for the biotech industry, is its reliance on two unreliable sources of funding. One is the equity market and the other is collaborative funding from big-pharma.
(Company 4: CFO)

Given the financial uncertainties, it is important for big-pharma to reinsert itself into the business model, and that is as a portfolio investor. I think that is something that big-pharma could be very good at. (Company 2: Vice President)
However, big-pharma funding of bio-pharma can bring with it a particular set of new problems. Specifically, one SME bio-pharma’s executive spoke of the necessity of balancing their big-pharma collaborator’s interests versus developing their pipeline of other products. Whilst the latter is regarded by the financial markets as more newsworthy, managing collaborator interests is also vital.

One major problem connected with equity funding relates to the composition of the bio-pharma shareholder base. Bio-pharma firms’ share prices are often volatile, particularly if the percentage of retail investors looking for short-term gains is high. Similarly, the NASDAQ quoted firm experienced large trading volumes although the CFO attributed this to the involvement of hedge funds. Another UK bio-pharma CFO also stressed the short-termist pressures exercised even by professional investors where:

"Most investors are interested in big discounts [on an equity placing] and professionals [i.e. investors] will flip out and get a quick return."

(Company 8: Executive Vice President)

There was only one firm interviewed which benefited from the particular composition of its shareholder base. In this case, the CFO was of the opinion that his firm was fortunate because investment in the company constituted only a small portion of the shareholders’ overall investment portfolios. Consequently, these three institutional investors were able to adopt a more sanguine view in the face of short-term share price volatility.

A number of those interviewed were positive about the contribution of disease-specific charities to the bio-pharma business model. Charities are able to provide support with expertise, network building and access to funds which do not dilute existing equity stakeholders. Such involvement by disease-specific charities is thought to strengthen the business model:

"I do think there are some powerful lessons to be learnt from leveraging relationships with disease-specific charities as I think here... we’ve done that extremely well in terms of accessing cash, which is one
thing but that’s only part of it because [of] the access to scientific know how and also gaining enthusiastic momentum. (Company 5: Rescue Consultant)

Matching grants with charity funding, according to one interviewee, helps consolidate financial resource and business intelligence about product to be developed in specific therapeutic areas:

...the charitable sector, because they often have funds that they are prepared to put down to projects, but very often if it could be matched in some way there could be a way of this central loan fund to use the intelligence that’s out there through these charitable sources, because the actual volume of knowledge that is available to the City in this sector is constrained. (Company 5: Rescue Consultant)

It is clear that the existing complex funding model has not been functioning efficiently and effectively in recent years. There has been a rapid reduction in equity and private venture capital funding. To quote one bio-pharma CEO:

In the UK, we have a very free market view of things, so that here you’re thrown to the wall, the view being that this toughens you up. (Company 7: CEO)

Many SME bio-pharmas are running low on cash reserves and so are cutting back on product development, slowing development and focusing on fewer projects:

We’ve had to manage the cash flow on a daily basis to keep the company moving. (Company 1: CFO)

This bio-pharma CFO continues:
It’s the old type of 80:20 thing. Cash flow management should take 20% of your time and actually now it’s taking 80% of my time. (Company 6: Executive Chairman)

Another SME bio-pharma director comments on the very real effect of such capital shortages:

...we have a platform technology where... it’s a gene delivery system. If you put a different gene in, you can make a different product and treat a different disease, and there are a dozen other things that we could do with that platform. We have had to focus on doing, you know, one or two things rather than developing across a broad front. And again, if capital had not been a limiting factor, you know, if there had been a model that said it’s understood that you need a range of products because not all of them will work as well as you think, and you need a long time window to plan to do it properly, if that perfect funding environment existed, our business would be different from how it is now. (Company 4: CSO)

Instead, despite firms’ desired strategy to develop a balanced portfolio of products, the market will often persist in focusing on one drug, to which it ascribes 95% of the firm’s value.

Other effects of such capital shortages include the following:

We’ve done quite a bit of work last year trying to look at our focus, rationalise which things are worth keeping. (Company 5: COO)

So we were hanging on by our fingertips though 2009, doing a lot of things that we didn’t like to, but had to do in order to save cash, so that we were still around when we got the results. (Company 5: COO)

I would present the accounts and say, well, we’ve saved £100,000 against budget and he [a fellow director of this SME bio-pharma]
would say, well, that’s not much of a success because it means we’ve
done £100,000 less in our R&D, and as long as you’re confident that the
sort of capital to fund it is there, you should spend, spend, spend. But
unfortunately, you know, we have to be much more cautious because
there is very little certainty of resources, of funding. (Company 4: CFO)

In the current environment, [we] go for stuff further down the
[development] pipe [line]. (Company 5: CEO)

Some bio-pharmas are now forced to re-think their strategic priorities
and build new investing networks and relationships:

I think those that are short of cash – there are many of them out
there, from those that we’ve talked to – are not articulating their
positions strategically in this sort of way. There’s this, sort of, you
know, desperate need for cash but not articulating how and in what
way it’s going to bring the asset base and the business forwards, nor
how we can constitute the value of that asset base through developing
new networks and relationships. (Company 5: Rescue Consultant)

Others are selling knowledge assets at a discount to keep going:

When that window starts to look short, you get back in and get some
more and take a very commercial stance. I think the real big thing is,
for example, we’re looking at partnering something at the moment, it
might not be the deal we’d always hoped for but actually, does that get
us where we want to be to do the next thing we want to? Everybody
in the building would say to me, ‘We’ve had this baby for 13 years. Oh
my God, you can’t give that away for that’. I don’t give a damn, if it
gets me from here to there and lets me do the next thing I’ve got to do.
(Company 4: CEO)

And those that have secured some funding in a difficult financial
market find themselves in a position to exploit the low market valuation
of firms that have intangible value in their product development
pipelines. For one company executive recently flush with cash funding from a recent placing, the financial crisis is an opportunity:

Yes, I mean it’s been good for us; it’s made other companies available for sale, a lot of programmes available for sale, which wouldn’t necessarily have been available. I mean we were lucky in that we raised the money, so we were able to take on that side, but we’ve been positively affected because of some of the things that we can buy. (Company 10: CFO)

In the next section, case studies reveal how these issues play out in a range of individual companies.

Company cases

Six company cases are chosen for this final section because they represent a broad range of therapeutic research areas, age profile, growth strategies and ownership (private and publicly owned).

Spin-out plc

Spin-out was formed in the mid-1990s by an academic, an internationally recognised authority on gene expression and retrovirus research. This professor acted as CEO until 2008 and then stepped down in order to act as chairman. A new highly commercially oriented CEO, a non-scientist, took his place. Growth to date has been organic for this spin-out company but recently the firm has become much more development-focused whereas in the past it concentrated on pure research.

Spin-out specialises in gene therapy and immunotherapy for addressing diseases in the fields of oncology and neurotherapy. Regarded as one of the leading companies in these fields, the firm’s strategy is to realise the potential of its innovation through both in-house and collaborative development.

In 2009, Spin-out’s R&D activities were focused on three key areas: prostate cancer; Parkinson’s disease; and ocular programs. Additionally, Spin-out maintained its significant investment in its major technology
platform and it continued to work with various academic groups and disease specific charities as a cost-effective and non-dilutive means of funding early-stage development. Average head count for 2009 was 69 with 58 being in R&D, these staff being mainly UK based although the firm had a continuing presence in North America.

By late 2009, Spin-out had raised £100 million of equity funding and roughly £30 million of partnership funding but accumulated losses amounted to around £100 million of which R&D expense constituted over 90%.

A major problem faced by Spin-out concerns the long development cycle of drugs versus the short-term nature of the funding by capital markets. This leads to serious dilemmas for the firm. In order to conserve cash, one Spin-out executive comments that if necessary, the firm would cut back on R&D expenditure:

...but it’s sort of a living death. (Spin-out CFO)

Compromises and short-term adjustments have to be made and so managing news flow is crucial, the Chief Scientific Officer (CSO) commenting that this substantially affects the type of R&D activity undertaken by Spin-out. Specifically, this translates to a certain extent into pressure to find diseases where a significant difference can be made within a short time frame. One Spin-out executive comments:

So you’ve got tensions between technology and the demands on news flow and return. (Spin-out CEO)

Additionally however, the firm faces other pressures to balance the interests of its major collaborator now providing partnership funding.

Neurobiotech plc

Neurobiotech was founded in the mid-1990s by a group of individuals, one of whom remained as CEO until 2006. Originally the firm was focused on functional foods, defined as food which has medical as well as nutritional benefits. It was the original intention that
revenue from functional foods would fund research into conventional pharmaceutical drugs. At first, the firm’s planned route to market was to start with plant extracts and health foods and then develop plant-based medicines, isolating the active chemical and to test for proof of concept and develop into a pharmaceutical product.

This strategy was modified after withdrawal of support, in 2008, from a major multinational with whom Neurobiotech was collaborating. Accordingly, in 2009 the firm undertook a strategic review first reducing head count by 50%. New network initiatives (sponsored by external consultancy) centred on working with disease-specific charities to strengthen expertise and some additional funding was also found which did not dilute equity. Attention was focused on Parkinson’s disease with the company re-inventing the focus of its products:

*The other thing is, which I think is perhaps quite useful for small sectors, is that what we have learnt from the last 18 months, two years is that it’s not just getting the money from these grant bodies, it’s actively developing a networked relationship with them. Because they’ve got some very knowledgeable people about that specific disease area, they have enormous commitment to that area and they are very thorough, going through things with a [fine] tooth comb. So that building some credibility in the scientific aspects with these disease specific charities also gives a lot more credibility in talking to these senior advisors. (Neurobiotech CEO)*

Despite these very real achievements, the company was running low on cash resources and was not in a position to finance Phase II clinical testing. A search for further funding was strengthened by the support of disease-specific charities, a new network of panel experts and a ‘lean out-sourcing’ business model presented to equity investors. At the end of 2009 Neurobiotech was successful in raising £25 million of funding to take its Parkinson’s disease product into Phase II trials. The immediate impact of securing additional funding was to increase the share price from 5 pence to 25 pence per share and although this has gently reduced it still remained at 10 pence per share a year later (Chart 12).
Privateco was founded in the late 1990s by an ex-senior manager from big-pharma together with two academics. The new firm did not start life as a university spin-out, instead it began life with no intellectual property (IP). The ex-big-pharma senior manager acted at first as Privateco’s VP of research but has since been appointed CEO. The firm’s growth to date has been largely organic.

The firm’s main activity is fragment-based drug discovery using a range of high-throughput biophysical and computational techniques including X-ray crystallography. The company’s unique approach has enabled the generation of a pipeline of novel small molecule drug candidates which the firm is advancing independently and through collaborations. The firm’s internal pipeline is currently focused on the discovery and development of products in the therapeutic areas of oncology and anti-virals. Most of the firm’s clinical trials are carried out in North America.

Privateco’s pre-eminent position in this field is underlined by:
• The productivity of its discovery engine which has delivered five novel drug candidates into development in four years – three of which are now in clinical trials with another two in preclinical development.

• Multiple collaborations in various therapeutic areas with big-pharma that collectively have a headline potential deal value in excess of $1.6 billion for Privateco.

• World-class science that has been published in leading journals such as Nature, Science and the Journal of Medicinal Chemistry, with some of the firm’s papers being among the most cited in their field.

To date Privateco has raised over £80 million of equity funding and partnership funding to underwrite R&D spending of roughly £11 million per annum. Overall accumulated losses were recorded at around £66 million for the year end 31st December 2009. However, revenues from licence fees and income from partnership agreements generated sufficient income to cover annual R&D spend in 2009 and the firm also had positive cash reserves.

The firm’s investors come from various institutions including venture capital partners, big-pharma firms and the local university. To quote one Privateco executive on his relationship with investors:

You know, specifically with my VCs, the overall goals are aligned. You know the management team and the VCs want effectively, the same thing. (Privateco CEO/CSO)

But the demand for a return on capital funding has become more pressured. To quote one Privateco executive:

Yes I mean specifically in our case because of how long we’ve been going. You know, we have a… 10 year shelf life and then you know, I mean you can get extensions for a couple of years... their business is to get a return on investment. (Privateco CEO/CSO)
Although privately owned, the firm is still required to manage news flow carefully, the CEO estimating that he spends at least one third of his time engaged in communication.

CNSbiotech plc

CNSbiotech plc was founded in 2003 by an academic who became the firm’s Chief Scientific Officer. Growth to date has been both organic and acquisition-based, the firm acquiring a private company and a publicly quoted firm in 2009. As a result of buying these firms, CNSbiotech acquired a suite of relatively advanced programmes. The firm also has a services business so that in its early years, net cash outflow was minimal despite significant R&D spend.

CNSbiotech specialises in diseases of the central nervous system (CNS) including Parkinson’s disease, epilepsy, cognitive impairment and neuropathic pain. The CNS comprises the brain and spinal cord and so controls all body functions and endows humans with consciousness, personality and intellect. In 2009, the firm made the transition from previously specialising in the development of medication targeted mainly at neurodegenerative diseases to focusing on drug development in the wider areas of diseases of the brain and CNS. In the area of CNS, the firm has the capabilities and financial strength of a much larger company.

The firm has the following strategic priorities: expand its pipeline through acquisition, in-licensing and partnering, acquire marketing rights to develop to value inflection points, reduce duplication costs through consolidation and integration and finally secure partnership agreements with big-pharma in its specialist areas.

The firm was floated on the AIM market in 2005 and raised over £10 million at IPO and by early 2009 had accumulated losses of over £10 million. Despite difficult market conditions, the firm managed a substantial fund-raising event in 2009 of £50 million.

This funding has been earmarked to finance a series of acquisitions and the development programmes secured through these purchases. The CFO put the success of the fund raising of £50 million in 2009 down to the fact that big shareholders believed in the strength of the firm’s
business model which the CFO characterises as being probably less risky than that of its peers, focusing as it does on acquisitions, risk sharing, collaboration and partnerships.

*With acquisitions, we have some other products that may be useful in neuroscience but may be useful in others as well so you can have a drug that is useful for multiple sclerosis, which is neurodegenerative, but the same drug may be useful for infections or immunology. So our drugs have more than just one indication.* (CNSbiotech 10: CFO)

**Chart 13  CNSbiotech market value to total investment (IPO/Refinancing) ratio**

For most of the period since IPO, CNSbiotech market value to investment ratio drifted on a downwards trajectory and remained below the ratio for all AIM listed bio-pharmas. By the middle of 2008 the market value to investment ratios converge but thereafter, until Spring 2009, CNSbiotech moves ahead of the all AIM bio-pharma (survivor) market value return on investment ratio.
This financial performance coupled with its aggressive acquisitions strategy to build its product portfolio, may explain why CNS-biotech was able to raise additional funding of £50 million in a difficult market in April 2009. However, this only served to force equity investment ahead of market value, dragging the market value return on investment down to a ratio which was below the average for AIM listed bio-pharmas at the start of 2009, before recovering towards the end of 2009 (Chart 13).

Devco plc

Devco was formed in 1997 as a spin-out from a major university by an academic at that institution. Growth to date has been largely organic but like Spin-out plc, the firm has become much more development focused whereas in the past, it also undertook research. Devco was listed on AIM in 2006.

Devco specialises in the development of high value biological compounds and vaccines. The firm limits its scientific efforts to providing application support of its intellectual property (IP) to third party collaborators with a view to the partners undertaking the full costs and risks of clinical development of their product under licence of the relevant technology. The company’s model does not include the funding of clinical trials.

_The nature of our business is not that we are drug developers. We are not going to (the) markets and saying, give us $10 million or $20 million to conduct a clinical trial. Our management objective is... working with third party collaborators on the application of the technology for their specific indications, so the pacing ability of us internally to rule out the technology is limited to a very significant degree by the ability of our collaborative partners to develop products through clinical applications._ (Devco CEO)

Accordingly, the firm’s business model has a much lower risk profile than those of most early stage life science companies. The firm’s intellectual property is not indication specific but rather, targeted at a wide
spectrum of applications in biologics and vaccines. Platform technologies allow the firm to partner specific applications and therapeutic areas, so allowing Devco to licence each technology to many partners. Devco’s platforms for drug development and vaccine development are used in development projects by a range of big-pharma companies.

Devco’s super generics pipeline contains a range of new product candidates which are currently under development, either in-house or with biotechnology and pharmaceutical partners. These new products in Devco’s pipeline have the potential to access a market of several billion dollars. The new products are based on Devco’s proprietary drug and vaccine delivery technologies and have been developed to offer improved performance and delivery. Devco’s unique delivery technologies have the potential to create new high-value, differentiated proprietary products from off-patent actives.

By late 2009, Devco had raised roughly £9.3 million of equity funding relative to its market value of £15.2 million which at 1.6 is below the average for the survivor group of bio-pharmas of 2.5:1

**Chart 14 Devco plc investment and market value return**
At the end of the financial year December 2009 Devco Plc had cash reserves equivalent to just 3 months of R&D expenses. In April 2010 a successful placing raised another £1.2 million providing another three months of cash burn breathing space.

**Newprivateco**

Newprivateco, a drug discovery company, was founded in 2007 by a group of pioneering scientists as a spin-out from a world class laboratory based in the UK. The company has a founder management team of the CEO and a Chief Scientific Officer who combine expertise in structure-based drug design with experience of drug discovery and development.

Newprivateco is focused on novel small-molecule drugs targeting a specific group of protein-coupled receptors. The firm's strategy is to leverage the unique opportunity its particular technology and drug discovery capability offers in three ways: firstly, to develop a pipeline of first-in-class drug candidates directed to selected protein-coupled receptors as potential out licensing opportunities; secondly, to seek strategic partnerships with pharma and/or biotech companies to identify leads to designated protein-coupled receptors or families in specified disease areas; and thirdly, to identify partners with which to develop therapeutic antibodies with a specific activity for target protein-coupled receptors.

To date Newprivateco has made progress with several protein-coupled receptors and in 2009 entered into an agreement, potentially worth more than $200 million, to apply its particular technology to generate novel drug leads against a protein-coupled receptor of interest to a major pharmaceutical company.

By the end of 2009 Newprivateco had raised over £10 million of equity funding relative to accumulated losses of £5 million and thus cash reserves were £4.5 million and equivalent to just over one year’s worth of R&D spend.

The CEO is critical of changes in tax rates for venture capital partners and how this could discourage investors.
The lower rate of capital gains tax (CGT) at 18% was critical in that founders and others were able to share in the risk and growth of biotech firms when these individuals decided to turn their backs on stable and secure jobs. CGT now at 50% is in effect treating you like you haven’t really earned the money whereas small biotech firms really do create the wealth. (Company 7: CEO)

However, despite its recent success in fundraising, the CEO comments that the capital available to UK biotech firms is less than in other European markets, such as Switzerland. He emphasises the need for biotech firms to show evidence of at least one success in drug development if they are to raise sufficient capital for their needs. Otherwise, to quote the CEO, ‘You’re only putting enough petrol in the tank to go half way’.
4. Key findings

Key findings of the study are as follows:

• The bio-pharma business model is complex and depends on innovation and re-invention to help secure favourable milestone reports, follow-on equity funding, and higher stock market valuations to keep it all going.

• As the financial crisis deepened during the period 2007 to 2009, the average AIM listed bio-pharma’s market value dropped by two-thirds. IPO’s and follow-on equity funding dried up (see Chart 11).

• Managers reported spending a greater proportion of their time on project management so as to reduce ‘cash burn’. They also report rationalising of products in the pipeline and slowing development to reduce total costs (see Chart 4).

• The report’s analysis reveals that one-third of AIM listed bio-pharmas had less than 6 months of cash burn available at the start of 2010.

• Investors managing a portfolio of AIM listed bio-pharmas would have generated a strong market value return on total investment (IPO and equity follow-on funding) relative to an average AIM investment portfolio.

• An average investor placing bets on all AIM listed bio-pharmas listing on AIM since 1998 would have invested IPO and follow-on funding totalling £2.5bn and generated a market value return of £5bn as at June 2010 (see Table 1).

• Capital at risk is surprisingly low in AIM listed bio-pharmas but the scarcity of following on funding and the aftermath of the financial crisis threatens to undermine the complex stakeholder network that sustains innovation and re-invention in the bio-pharma business model.
5. Recommendations and policy changes

This report reveals how the financial crisis has modified management and investor behaviour within the SME bio-pharma business model. Managers have significantly cut back on development expenditures, putting projects on hold, reducing the volume of product in pipeline and selling off assets to secure cash funding.

Investors are coming back into the market but they are generally investing in products in a later stage of clinical testing because at least these products have passed initial screening tests and so promise a more secure financial return. Products that are at an early stage of development, for example at early spin out or first stage clinical trials, are receiving less attention from managers and investors. Early stage development is considered to be a riskier investment opportunity because regulatory approval and a financial return are distant and uncertain.

Adverse changes in the public and private funding climate and modified priorities of SME bio-pharma managers means that it will be much more difficult for UK universities and medical research centres to spin out and fund early stage product development.

This report presents both short-run and medium-term recommendations.

Our first short-run recommendation:

Government funding must continue to sustain early stage research and product development in universities and medical research centres.

The cuts to university and research institute funding could undermine the UK's capacity to develop new pharma product and the flow of spin-out investment opportunities.
Our second short-run recommendation:

There is a strong case for government emergency funding where this can sensibly prevent a disorderly downsizing of bio-pharma SMEs. After the 2007 financial crisis a significant number of SME bio-pharmas exited the AIM because they had run out of cash. Risk aversion and a lack of liquidity from investors may explain this to a significant degree. However, once in administration, it is very difficult to recover value from intangible assets that depend on retaining highly skilled employees and maintaining a complex stakeholder network.

Our medium-term recommendations:

Our recommendations draw inspiration from one of our interviewees who raised the following question:

‘Where does UK bio-pharma want to be in terms of a player?’
(Company 2: Vice President)

The question we have to address is: where is the real competitive know-how of the company and what should be shared for the common good? I think that’s a big discussion. (Company 2: Vice President)

The bio-pharma business model is facing a significant test of viability as big-pharma revenues decline in highly contested markets and downsizing is forced through to protect shareholder value. Big-pharma will, as a result, globalise R&D into regions that promise low cost rapid product development and testing because this will help close the gap between ‘financial tolerance’ and ‘development time horizon’. This threatens to undermine the viability of the UK SME bio-pharma business model.
The objective is to:

*Re-draw the way in which the bio-pharma business model is financially supported and how risk and return are distributed between the different stakeholders involved in a complex development network – working back from patient neurology into the university/medical research lab.*

(Company 2: Vice President)

The UK SME bio-pharma business model must adapt and evolve. Elements of this evolution might include:

- Access to NHS clinical datasets to provide a significant knowledge resource to strategically drive drug discovery.
- Government funding to UK universities and medical research institutes balancing academic standards with a sense of commercial urgency.
- Open innovation investment consortia to spread financial risk that is inherent in long complex development and testing value chains.
- Regional network groups that could provide advisory services and mentoring support to the stakeholder network that supports the bio-pharma development chain.

Adapting the SME bio-pharma business model for a sustainable future will be a challenge. Innovative policy interventions, clever regulatory arrangements and imaginative funding mechanisms are required. The purpose is to secure bio-pharma’s contribution to UK national output, employment and balance of trade.
References


Appendix 1

Outline interview questions posed to SME bio-pharma executives

Chief Financial Officer (CFO)

Question 1
Would you say your company requires frequent re-financing? To what extent have you managed to refinance your development from your own funding?

Question 2
How important are milestone reports/announcements on pipeline progress?

Question 3
Are your firm’s investors focused on particular pipeline products or progress of the whole portfolio of products in your pipeline?

Question 4
To what extent are your investors loyal and committed?

Question 5
Has the financial crisis made it difficult to obtain re-financing?

Question 6
Has this slowed down your development schedules? Have you been required to rationalise your pipeline?

Question 7
In terms of strategic financial performance of your firm – could you tell me what are the main financial performance or key financial performance measures you employ? To help you guide the business and inform stakeholders about your performance?
Question 8
Do you find that there are increasing pressures from your shareholders to improve their returns – in terms of share price? Do you expect pressures at some point in the future to pay dividends?

Question 9
At the shareholder/investor meetings what do you see as the major concerns emerging from these discussions? e.g. competitive pressures, exchange rates, or the launch of new pipeline products?

Question 10
How important is it to senior management that this financial strategy and future performance is reflected in the share price and a strong buy recommendation from analysts?

Chief Scientific Officer (CSO)

Question 1
Over the past few years how and in what ways do you feel the function of R&D within your firm has changed?

Question 2
What things are easier and what things have become more difficult for you within the R&D function? How have the challenges changed?

Question 3
Do you feel that the company has become more cost and profit conscious? Has this been reflected in the development of new financial control and planning systems?

Question 4
Are you set any performance targets or financial ratios (KPIs) which are key measures of performance – do you feel these are appropriate or could improvements to these be made?
Question 5
Do you feel that the pressures to improve margins and returns on R&D investment are forcing you to think about new ways in which you might organise the R&D activity – e.g. in terms of project management and/or the location of development and testing of new products?

Question 6
What performance measures are applied to R&D – could be simple profit targets, share of revenue from products introduced within say the last 2 years, number of patents registered, R&D costs in themselves or as a proportion of other measures? Projects in the pipeline? Anything else?
About the authors

Professor Colin Haslam is Director of the Finance Accounting Research Unit (FARU) within the Business School at the University of Hertfordshire. He has acted as member and chair of the Business and Management studies panel for the Academy of Finland Research Council during 2010 and has also been appointed member of European Financial Reporting Advisory Group [EFRAG] ‘Disclosure Framework Advisory Panel’ Brussels 2010-2011. His research focuses on the viability and sustainability of business models and this work will appear in a text commissioned by Routledge Redefining Business Models: Strategies for a Financialised World (2011)

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About SATER

The research projects which culminated in this publication were funded by grants from The Scottish Accountancy Trust for Education & Research (SATER) – a registered Scottish Charity (SC034836). The SATER Trustees are pleased to have been able to support these projects and hope that the results are of interest and relevance to a broad range of users.

SATER’s objective is to promote research into, and education of, accountancy, finance and management together with all subjects in any way related. In fulfilling its charitable objectives, it also seeks to provide public benefit by making grants for research projects which result in reliable evidence for use in the development of policy – by professional bodies, standard setters, regulators or governments.

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The Trustees would like to thank the ICAS Research Committee and Research Centre staff for their support, through liaison with the academic team and the provision of advice and assistance at various stages of the project. Their role in reviewing publication drafts and providing constructive comments to the authors has been invaluable in producing publications which are easily accessible and of interest to ICAS members, the interested public and policy makers.

Further details about SATER and the ICAS research programme can be found from the SATER and ICAS websites: scottishaccountancytrust.org.uk/research.html and icas.org.uk/research.

David Spence
Chairman of SATER
July 2011
We all rely upon medical and scientific advances; however, because of the risks intrinsic to research and development, the associated funding is inherently risky as well. How does the bio-pharma industry operate and how has the industry been affected by the financial crisis? The UK government provides significant financial support to the bio-pharma sector in the form of research and development tax credits and is again targeting the pharmaceutical industry as a key driver of UK economic prosperity. The coalition government has recently issued a consultation document “patent box” where the objective is to provide financial incentives to develop and exploit bio-pharma intellectual property in the UK.

This study investigates the UK SME bio-pharma sector. It tracks AIM listed bio-pharmas to investigate return on investment and the level of capital at risk, considers the impact of the financial crisis on the sector, and seeks the views of senior executives of private and publicly quoted bio-pharmas and industry representatives. The study concludes by presenting the case for innovative short and medium term government-led policy initiatives for the sector and highlights four central areas in which the current bio-pharma business model could evolve.

EAN 9781904574798

Price: £10.00