Beyond the Magic Beanstalk: A study of life science ecosystem formation at the university-industry boundary

University of Edinburgh Business School
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Preliminary study report

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Introduction

This preliminary report presents the early observations and analysis from a multi-year study of the life science ecosystem centred on the University of Edinburgh College of Medicine and Veterinary Medicine. It incorporates market study work conducted by the Edinburgh BioQuarter and ongoing research at the Centre for Entrepreneurship Research at the University of Edinburgh Business School.

Connections between the fields of medicine and business management are, historically speaking, a relatively new phenomena. The rise of the pharmaceutical industry on a global basis, the promise of biotechnology, government funded foundational research and the expansion and consolidation of the health services and insurance industry in the United States have led to unprecedented investments in life sciences. Although the predominance of revenue and profits in these fields is generated by large, increasingly transnational organizations, government and educational institutions have found inspiration in the entrepreneurial stories of innovative, high growth life science ventures. To be sure, the job creation and tax income value of these organizations is only realized after they grow out of the entrepreneurial stage, but universities and policymakers have often found better levers of influence in the creation and support of *de novo* firms.

The complexity of foundational research, product development and regulatory frameworks generally requires most life science companies to subsist on external finance, such as venture capital, for many years prior to market entry. In contrast to high-growth firms in the software and internet sectors which may experience explosive growth within a few years of launch, the cultivation of life science companies requires long runways and investor patience. In theory, this would appear well-aligned with the strategic vision of research universities. The institutionally-driven evolution of technology transfer capabilities at universities sometimes results in monolithic treatment of life science innovations, based on relatively short-term expectations for recouping patent filing and administration costs.

In this context, we initiated a multi-year study of the ongoing development of the life science ecosystem in and around the College of Medicine and Veterinary Medicine (CMVM) at the University of Edinburgh. CMVM is, in both research and practice, one of the top medical institutions in Europe. To complement its research and clinical capabilities, a significant investment by the University and the Scottish government has created the Edinburgh BioQuarter to support university-industry engagement and innovation commercialization. This appears to present some of the key resources and capabilities associated with the very early stages of a life sciences economic cluster.

The study has both research and practice-driven goals:

1) Chronicle the development of the ecosystem during formative stages,
2) Address relevant research questions about entrepreneurial behaviour within a large-scale institutional context
3) Test some of the extant organizational and entrepreneurial theories about innovation management and venture formation at the university-industry boundary

4) Provide advice to researchers, administrators, entrepreneurs, and policymakers on how to facilitate successful commercialization activities that benefit all stakeholders: universities, entrepreneurs, industry, and society.

This report presents some of our preliminary findings. Although we believe our observations and preliminary conclusions are well-founded, they are subject to revision as the study continues. The study is scheduled to conclude in late 2013. A final report will be published in late 2013 or early 2014 to present summary findings.

The Context: the UK biotechnology industry today

As of 2012, the outlook for biotechnology in the UK and Europe may appear less than secure. Overall employment in UK biotech has remained static for nearly ten years.[1] Some regions have experienced declines in biotechnology-related employment, usually due to the loss of a single significant organization. One example was the departure of Merck from central Scotland in 2009 with the loss of more than 250 jobs. The global financial crisis has had severe short-term effects on the global biotechnology capital market. Private investment in new biotechnology ventures fell from US$2.75 billion to US$ 2 billion between 2009 and 2010,[2] and only half as many new firms were funded in 2011 as in 2010. As is common during economic downturns, venture capitalists focus on managing investment portfolios rather than risking significant capital on new ventures. The repercussions of near-term resource constraints for early stage biotechnology ventures will be likely last many years. In the near-term, there will be fewer high-growth potential life science companies. In the long-term, there may be fewer large-scale exit events that generate high investment returns for the VCs and fewer "portfolio" entrepreneurs who start and fund related, follow-on ventures.[3]

Notwithstanding these challenges, life science research remains vibrant worldwide, and the social and economic impact of medical technology has never been more apparent. Successful innovation generates significant rewards at every stage of the technology development cycle. The global consolidation of the pharmaceutical industry means greater rewards for drug discovery and biotechnology firms that feed the drug development pipeline or provide the tools to make the pipeline more efficient. Entirely new business models for the provision of health care in developing nations target large, previously inaccessible markets. In addition, the continued development of life science research generates opportunities for related businesses that build on complementary capabilities. FIOS Genomics, for instance, is technically a data analysis company, but it combines 50 years of research and management expertise from the University of Edinburgh spanning genomics, pathway medicine and computer science to deliver bio-statistical datasets to its customers.

Broad economic trends aside, there are indications of support for the industry from the UK government. In the 2011/12 budget, Chancellor George Osbourne announced an increase in R&D tax credits from 100% to 225% for science-based firms; a decrease in corporation tax from 28% to 23%; and an increase in the tax-free allowance to

[1] Source: DTZ Ltd, 2011 (private research for UK biotechnology companies)
[2] Source: *BioWorld Today*, Tuesday March 29, 2011, "Biotechnology seeks alternative funding models"
[3] Source: Rosa, P (1998). *Entrepreneurial Processes of Business Cluster Formation and Growth by 'Habitual' Entrepreneurs.* Entrepreneurship Theory and Practice, 22 (4): 43-62.

angel investors in scientific companies from £2 million to £10 million.[4] Such measures are likely to increase access to resources for the development of the UK biotechnology industry.

Facilitating the development of sustainable life science clusters, or ecosystems, remains an important challenge for realising both the social and economic benefits of biotechnology. The "triple helix" model linking university-academic-industry collaboration to the development of local and regional knowledge economies presents an attractive and intuitive mechanism for explaining the development of such clusters.[5] Realistically, however, the anecdotal success of a handful of high-profile clusters, such as San Diego, Boston, and Medicon Valley (Europe), must be understood as exceptions rather than exemplars. Professor Anne Miner, an internationally-recognized management and entrepreneurship scholar, describes these cases where university technology transfer has directly and significantly impacted regional economic development as "magic beanstalks." She cautions that examples of limited success and near-term failure are far more prevalent.[6] Growing the beanstalk requires more than simply scattering seeds of new ventures randomly into the market. At the core of success is a cost-effective and efficient model for translating findings from research conducted at life science research facilities into viable products and services.

Success, then, requires talent, determination, and some good fortune. There are many lessons to be learned from successful programmes; implementing best practices increases the likelihood that good fortune may be capitalized. The resources and processes that support the beanstalk, even without the "magic," provide a foundation for the creation of high value-add organisations and the development of important new technologies and treatments. These elements form a constellation of assets that benefit patients, the healthcare industry and the economy.

The unreliable magic of university-based technology transfer

The scientific and economic impacts of university-based technology transfer are significant. As examples, Northwestern University received $700 million for the rights to the therapeutic Lyrica,[7] and Stanford earned $336 million from the sale of Google stock obtained in the spin-out licensing process.[8] In 2010, more than 5000 licenses were executed, 500 new start-ups were formed, and nearly $3B in total revenue generated by American university technology transfer offices.[9] It is not surprising, then, that innovators, university administrators, and policy-makers often look to research-based academic institutions as both hubs of innovation and potential drivers of regional economic development. As most research universities derive

[4] Source: *The Evening Standard*, 24 March 2011, "Chancellor announces good news for biotech firms"
[5] Source: Universities and the Global Knowledge Economy, edited by Etzkowitz, H and Leydesdorff, editors. 2002. Continuum International: New York.
[6] Miner, AS. et al (2000). "The magic beanstalk vision of university venture formation." In The Entrepreneurship Dynamic. (Eds. Kaye Schoonhoven and Elaine Romanelli). Stanford, CA: Stanford University Press.
[7] Mantone, J. (2007). "Pfizer's Lyrica Gives Another Boost to Northwestern." Wall Street Journal Health Blog, December 19.
[8] Krieger, L. (2005). "Stanford Earns $336 Million Off Google Stock." San Jose Mercury News, December 1.
[9] The Association of University Technology Managers (2010). "University Technology Transfer: Why We Do What We Do." www.autm.net accessed 1-May 2011.

funding from public sources, there is often an added perception that technology transfer offices (TTOs) at those institutions have a responsibility to generate economic outcomes to justify public investment. A few institutions seem to have fulfilled this potential, and are commonly interpreted as examples for the rest.

But in the world of university technology transfer, licenses and spinouts that generate millions of dollars in stock and royalty revenues for TTOs are outliers.[10] It is important to place cases like Google, Remicade, and Tomotherapy in context. The $2-3 billion of licensing income generated by American universities stems from roughly $55 billion of total sponsored research. And while many university technologies represent high potential innovations, most emerge from university laboratories unproven in any commercial context. The *technologies* licensed through university technology transfer, almost without exception, will require many years and millions of pounds to become commercially-viable *products*. In fact, the majority will never see the market at all.

Leadership in practice: Imperial College London

Ranked the 9th best University in the world in 2011, Imperial College London employs 68 fellows of the Royal Society, with 14 Nobel Prize winners and two Fields Medallists among former faculty. Through its equity investment arm, Imperial Innovations Limited, Imperial holds stakes in eighty companies with a total value of these stakes of more than £90 million

Since 2005, Imperial College London has created eight new life sciences companies with a total investment value of £18 million pounds at launch. One of these companies, Respivert, was sold to Centocor Biotech for £9.5million, netting Imperial a return of 470% over a three-year investment. In 2010, Imperial Innovations Ltd declared pre-tax profits of £5.5million, up 5% over 2009.

Geographical concentration: London is home to many of the nation's most highly regarded medical schools and research institutes, including Guy's Hospital, Moorfields Eye Hospital, University College London and the new UK Centre for Medical Research at Kings Cross.

Access to venture capital: London is one of the world's greatest financial capitals, with more assets under management than any other location apart from New York. Imperial Innovations itself is AIM-listed and has more than £90m invested in 66 companies.

Infrastructure and process: Imperial Innovations handles more than 350 innovation disclosures a year. A new ventures team handles these disclosures, turning them into embryonic companies if appropriate. New companies are then handed over to an investment team for further development before being launched, including the creation of senior management teams and acquisition of venture capital investment. Imperial Innovations also runs business plan competitions and manages an "Entrepreneurs in Residence" programme.

[10] Bock, AJ. 2012. "Technology Transfer" in (ed. Marvel) Encyclopedia of New Venture Management. SAGE Publications: Thousand Oaks, CA.

The mundane behind the magic

The promise of university-based technology transfer for generating sustained economic development has been labelled a "Magic Beanstalk" by eminent management researcher Anne Miner.[11] In a detailed study of technology transfer at universities in eight countries, Miner and her colleagues showed that traditional views about the university's role in knowledge exchange have changed to include direct economic value creation. Whereas extensive research demonstrates the economic impact of training students and knowledge dissemination via various communication and media, many universities have focused efforts on licensing technologies to extant businesses and *de novo* ventures. These represent more direct mechanisms linking commercial economic activity to university research, with the added potential benefit of generating financial returns for the institution.

But three myths underlie the "magic beanstalk" vision. The first myth is that *any* university can launch successful spin-outs and start-ups. The second myth is that job creation *inevitably* follows from university-inspired venturing. The third myth is that this type of venturing helps address *local* job creation problems.

In reality, the economic promise of technology transfer, is limited by a numerous factors. The majority of *de novo* venturing occurs in very specific fields: computer science, life science, and a narrow range of natural sciences. These types of firms have high failure rates, despite the benefits of university origin. And because these firms tend to emerge and develop in geographical clusters, the positive economic impacts of firm formation may not accrue to the local area of origin.

The reality of university-based technology transfer is not a fairy tale with an inevitably happy ending. First, with the exception of universities benefiting from one-off licenses for blockbuster therapeutics, the most successful technology transfer universities are generally those that have consistently invested extensive financial resources over lengthy periods of time. Institutions like Stanford, MIT, and the University of Wisconsin facilitate successful licensing and venturing practice with a small army of technology, legal, and development experts based on decades of history and experience. And while Imperial College London may seem like a newcomer to world-class status, Imperial Innovations has been commercializing technology for 25 years. Imperial, in particular, has benefited from the combination of significant financial investment, a culture that emphasizes the social and commercial impact of research, and an extraordinary network linking researchers to industry.

Beyond the magic beanstalk: an entrepreneurial perspective

University technology transfer benefits from both hard work as well as long-term investment in systems, infrastructure, and knowledgeable individuals. In addition, the development of so-called "clusters" or "eco-systems" depends on many factors.[12]

[11] Miner, AS. et al (2000). "The magic beanstalk vision of university venture formation." In The Entrepreneurship Dynamic. (Eds. Kaye Schoonhoven and Elaine Romanelli). Stanford, CA: Stanford University Press.

[12] Menzel, M. P., & Fornahl, D. (2010). Cluster life cycles-dimensions and rationales of cluster evolution. *Industrial and Corporate Change*, 19(1), 205-238.

***Leadership in practice:* Cambridge University**

The process of translation between university research and commercial firms doesn't happen overnight: despite the best will of universities, governments and investors, partnerships take time to mature. Cambridge University, perhaps Europe's most successful example of a bio-technology cluster, has had institutional support for bio-technology company creation since 1995. Since 2005, Cambridge has spun out eight life sciences companies with total first-round funding in excess of £12 million. All these companies are still trading, and many have secured licensing deals or additional rounds of funding.

Geographical Concentration: In addition to the university itself, Cambridge co-locates the Medical Research Council, Addenbrookes' Hospital with XXX beds, and the British Biological Sciences Research Council at Babraham. There are also two science and technology parks in the greater Cambridge area.

Access to Venture Capital: Abingworth, one of the world's leading Life Sciences Venture Capital firms, opened its Cambridge office in 1989. Other venture capital firms active in Cambridge include Advent, Amadeus, New Hill and Chord Capital. These companies are joined by three university funds that provide a total of £7.3 million of seed funding for early-stage ventures.

Support: Cambridge runs two student Entrepreneur clubs that run business plan competitions for students and postgraduates. Additionally, there are investment forums at Babraham and the "Access" consortium to allow early-stage biotech ventures access to up to £7 million of early stage capital. The biotechnology industry is also supported by strong local government network, including the Cambridge Technopole and the East of England Development Agency.

Critical Mass: with seven science parks, two hospitals, the world's leading university and eight active life science venture capital investors, Cambridge has the critical mass essential to successful biotechnology transfer between universities and industry.

Promoting the Entrepreneurial Spirit: A "Cambridge Phenomenon conference", held in Q4 2010, suggests that those working in Cambridge recognise that, despite its obvious advantages, the region still needs to improve to achieve world-class status as a bio-cluster, as one speaker puts it, "We may have many of the features of a Silicon Valley-type innovation ecosystem, but we are still not completely, "getting it." Centre for Entrepreneurship represents a significant commitment by the University to facilitating both entrepreneurial activity within the University as well as interactions with industry.

While the impact of a major research institution should not be underestimated, rigorous research has repeatedly demonstrated that organizational heterogeneity and broadly-based absorptive capacity in the form of extensive and dense networks of technologists, industrialists, financiers, and entrepreneurs are essential to cluster formation.[13]

[13] Zucker, L. G., Darby, M. R., & Armstrong, J. (1998). Geographically localized knowledge: Spillovers or markets? *Economic Inquiry*, 36(1), 65-86.

The clustering model and magic beanstalk rebuttal both approach the incubation and fostering of a life science cluster as a fundamentally *institutional* process. In this context, the critical drivers and leverage points are the policies and norms of the institutions played out against exogenous market forces and economic factors. To be sure, all entrepreneurial activity functions within these parameters, and some conditions are more conducive to encouraging economically desirable outcomes such as growth in skilled employment. But entrepreneurship is fundamentally an individual- and team-based endeavour. To ignore the role of the entrepreneur in the development of a life science cluster, especially at the university-industry boundary, fails to account for the idiosyncratic and creative potential of the people who will create and grow the cluster.

Extensive research has shown that financial incentives are not the sole or even primary driver of entrepreneurial activity at the university-industry interface.[14] In addition, the research on "inventing entrepreneurs," academics who participate in the commercialization of their own research, demonstrates the learning value associated with both successful and unsuccessful venturing. In other words, the measurement of near-term success or failure at the individual and institutional levels may not be the best indications of cluster formation potential or progress.

Although rigorous analysis on the financial returns to university-based venturing is still contested, other aspects of the impact of university venturing and industry engagement are emerging. Academic scientists who participation in ommercialization demonstrate an increase in high-quality research output, especially in the life sciences,[15] where the scale of resources required to progress fundamental research commonly requires multi-institutional collaboration. Second, life science firms struggle to expand into market areas too far afield from core skills.[16] This means that a constant influx of entirely new ventures is likely necessary in any given cluster to maximise the cluster's innovative capacity. Finally, the roles of uncertainty, experimentation and luck cannot be entirely eliminated from a given industrial cluster. New ventures must experiment with product, service, and business model innovations precisely because the success of such innovations cannot be ascertained ex ante.[17] In other words, it may be extremely difficult for policymakers and institutional administrators to align incentives with a tolerance for failure that facilitates high-potential venturing activity.

[14] George G and Bock AJ (2008). Inventing Entrepreneurs. Prentice-Hall Pearson: Saddleback, New Jersey.
[15] Research on academic scientist output.
[16] George paper on intuition
[17] Heirmann and Clarysse 2005.

Leadership in Practice: Oxford University

The oldest university in the English-speaking world, Oxford has spun out some 15 life science companies in the period 2005-2009, with around £60 million of private capital raised. Oxford's chemistry department alone is the largest in the developed world and can claim ten Nobel Prize winning chemists over the last eighty years.

ASSETS:

Geographical Concentration: Oxford is home to the John Radcliffe, a large tertiary teaching hospital, in addition to the university's biochemistry, biology, information technology and engineering faculties. Other research assets located in Oxford include the Institute of Molecular Medicine and the William Dunn Pathology Institute.

Access to Venture Capital: Oxford Technology has operated Venture Capital Trusts (VCTs) and Enterprise Capital Funds (ECFs) in the Oxford area since 1983, investing between £100,000 and £300,000 in early-stage private biotechnology companies. The IP Group, which began in Oxford, has supported many of the early-stage investments made in spin-out companies from Oxford University.

Support: Oxford has created three investment funds to support technologies to commercialisation: the Oxford Invention Fund, ISIS University Innovation Fund and the Proof of Concept Fund, totalling some £6.8 million available to researchers for early-stage development of commercial applications. Additionally, ISIS Innovations Ltd, Oxford Unversity's tech transfer unit, has set up the ISIS Angel Network, a not-for-profit company designed to present new opportunities to private investors.

An assessment framework for life science cluster development at the university-industry boundary

Cluster analysis based on traditional industrial organization economics derives from the seminal work of Harvard Professor Michael Porter. The role of the university in the initiation, cultivation, and development of a long time-horizon life science cluster requires a more flexible approach. Our study combines Porter's industry clustering theory with Professor Miner's framework for the university's idiosyncratic influence on cluster formation. As shown in the "practice leadership cases," we specifically focus on the following six factors as the starting point of our research and analysis:

1. **Geographical concentration**. The successful bio-technology cluster will have at least one academic research institute in close proximity to a clinical research institute, a teaching hospital and other vital resources, including imaging equipment and animal biology institutes

2. **Access to Venture Capital.** There will be more than one significant venture capital firm with a local interest active in the area. Examples of this outside the UK include Mission Bay in San Francisco, Cambridge, Mass., and Medicon Valley in Denmark and Skäne, Sweden.

3. **Support.** Local firms with IT and physical sciences experience will be able to provide new bio-tech companies with the necessary legal, financial and intellectual property services to assist in the creation and development of the new venture. There will be experienced accountancy personnel available to hire on a consultancy or permanent basis.

4. **Critical Mass.** There will be a critical mass of companies in the area which will deliver a talent pool of managers experienced in working in scientific companies, bench scientists at all levels of experience, a university providing graduates and post-graduate students seeking employment, and senior managerial talent in the local area who have experience of managing spin-outs.

5. **Quality of Life.** Whilst this factor may appear to be "nice to have", it has proven essential in persuading experienced and successful executives to relocate from elsewhere in the country and abroad.

6. **Entrepreneurial Culture and Capabilities. T**he influence of institutional, macro-economic, and industrial-economic factors can't be ignored. At the same tie, a significant component of a cluster's growth and resiliency is culture and capabilities framework in which nascent entrepreneurs operate. Ultimately, it is individuals and teams that drive commercialization activities, whether via licensing engagements or new venture formation. If the development of entrepreneurial capabilities is supported, and an evergreen community of commercially-savvy scientists emerges, new "inventing entrepreneurs" are more likely to initiate and maintain commercialization practice.

A study of cluster incubation at The University of Edinburgh

A history of research and clinical excellence combined with recent investments at the university-industry boundary present The University of Edinburgh's College of Medicine and Veterinary Medicine as a nascent, high-potential life science ecosystem. This study has been undertaken to document the early development activities within the University as well as the current activities associated with technology commercialization and industry engagement.

CMVM demonstrates world-class medical research and innovation capacity. The University of Edinburgh is rated first in the UK for clinical medical research and first in the UK for veterinary research.[18] It is rated third worldwide for stem cell research based on publication impact.[19] Scotland's research in regenerative medicine was rated first in the world as recently as September 2010.[20]

At the same time, university-based venturing in biotechnology in Scotland has been relatively limited. In the past five years, only one biotechnology firm has been spun-out of the University of Edinburgh, and six others from other Scottish universities.

[18] Source: HM Government Research Assessment Exercise, 2008
[19] UK Government, 2008 Research Assessment Exercise. See www.direct.gov.uk
[20] Source: Province of Ontario for the Canadian Government, September 2010

The Edinburgh BioQuarter is designed to encourage enterprise at the university-industry interface. In recent years, CMVM and the BioQuarter have invested in assets and capabilities to support engagement with industry. These notably include:

- A commercialization support team with extensive experience in biotechnology venturing and collaboration,

- New facilities including both commercial space targeted at extant life science firms as well as an incubator space for new ventures, and

- A collaboration with NHS and industry for an annual innovation competition to encourage and reward health-based innovations developed at the University and NHS with the potential to mature into new ventures

***S**ummary and study progress*

Research and practice demonstrate that the emergence and development of industrial clusters derive from complex and highly idiosyncratic institutional and economic factors. Explaining cluster formation in hindsight often appears logical, but facilitating and predicting new cluster formation remains art rather than science.

At the same time, the reality of cluster development processes likely falls somewhere between Porter's overly optimistic framework and Miner's cautionary analysis. To that end, there is much promise in the ongoing study to describe and assess the maturation of the nascent life sciences cluster centred on the University of Edinburgh's College of Medicine and Veterinary Medicine. Over the next two years, extensive data collection, combined with review of historical documentation associated with the establishment of the Edinburgh BioQuarter, will reveal both micro- and macro-level mechanism that support or inhibit cluster development. While some findings will likely confirm prior research and case study examples, the circumstances and resources at Edinburgh present a unique opportunity to test theories of cluster facilitation and maturation in real-time. In addition, the study plans to generate practice and policy implications for encouraging university-industry engagement in the life sciences, at Edinburgh and beyond.

The study is expected to conclude at the end of 2013, with a research report and policy summary to be produced in mid 2014.