Corporate venture capital and Cambridge

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A novel route to entrepreneurship at the University of Cambridge.

As the pressure on public funding continues to grow, academic scientists are increasingly contemplating the merits of a biotech spin-out venture to advance their research. The challenge today is that traditional venture capital has largely moved away from early stage innovations, seeking the safety of more developed, de-risked technologies for their portfolio pipeline. By contrast, the pharmaceutical industry has demonstrated a growing interest in this field and is now a major player in funding biotech startups.

Corporate venture capital (CVC) is nothing new in itself: Johnson & Johnson Development Corporation has been operational for 40 years, and most of the other pharmaceutical household names have similar mechanisms in place (Fig. 1). What is new is that now, with CVC playing a larger role, there is a need for streamlined processes to drive the generation of joint academic-industry spin-off entities within the human medi-

cine and drug development space. This article presents the findings of research carried out at the University of Cambridge to identify when a new academic discovery becomes venture ready, what makes a 'killer' CVC pitch and how to initiate preliminary collaborations around nascent venture discoveries.

Timing is everything

The kind of research that drives a new candidate along the drug development pathway to a commercial product is known throughout the scientific community as the 'valley of death'^{1,2} because it is complex, expensive, underfunded and outside the expertise of most basic scientists³. As such, when scientists want to engage in negotiations with a corporate partner concerning a spin-out, one of the most common questions is when to start. To answer this, we carried out iterative interviews with CVC directors from six pharmaceutical giants, spanning the original to the most recent (Johnson & Johnson, GlaxoSmithKline, Eli Lilly, AstraZeneca, Roche and Merck). All are actively investing today, so we asked them to rank the translational milestones that, in their view, should trigger the spin-out discussion. **Figure 2** shows a mismatch of expectations, with academics consistently over-rating the spin-out potential of a discovery relative to corporate venture capitalists.

By contrast, corporate interest is highly focused, with *in vivo* data on a lead compound consistently cited as the major trigger for venture discussion, as summed up by Marian Nakada, vice president of venture investments at Johnson & Johnson Development Corporation. "When a company has proof-of-concept data from *in vivo* animal models on a compound with drug-like properties, that is when we typically start looking at the opportunity as a potential series A investment," she said. Before *in vivo* data is available, corporate investors gener-

ally consider backing unproven technology only if the risk can be mitigated, usually by developing a platform with more than one clinical shot on goal. Syndicating is another de-risking approach common within the close-knit CVC world, although venture capitalists can struggle to find partner investors with only *in vitro* data. In the later stages of this spin-out pathway there is less flexibility: corporate venture capitalists are cautious about academically led clinical trials because often the compound has not been formulated for commercial use, raising concern that precious patent life will be wasted.

Pitfalls of the pitch

Having identified when a discovery is venture ready, we focused on the second major hazard for our fledgling entrepreneurs: how to turn their 20-minute pitch into a funding success. We started by asking our corporate venture capitalists to identify common academic stumbling blocks. Not surprisingly, understanding of the commercial process was flagged as the biggest challenge. The pitch is a bad time for academics to learn they have misjudged the maturity of their discovery, yet it happens regularly—even though it can be avoided by simply benchmarking against industry to determine how they would proceed. Doing so is not difficult; the people who perform research in industry are also scientists, trained in the same places and driven by the same dedication. "People in industry devote their lives to this; they are passionate, and they genuinely will help just because they are nice people. Academic scientists don't call to ask, and I don't know why," said one CVC director. Simply picking up the phone and asking about the industry standard for animal models or the names of potential collaborators at other universities can yield superlative results.

Other common pitfalls relate to misinterpreting the market landscape. For example,

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Figure 1 Timeline for CVC arms of big pharma. Not only have the CVC arms of the pharmaceutical giants continued to operate following the 2007–2008 financial crisis, but also more have been initiated as the pharmaceutical industry adopts an increasingly adventurous approach to investing in academic innovation. Fund value indicated when specified by the company.

although the scientific excitement may be entirely justified, a slightly lower dose or different pathway is not enough to differentiate a new commercial product. Defining the characteristics of a game-changing marketable trait, and then communicating how the discovery meets that need, is essential for a successful pitch.

A further checkpoint for academics is to ensure that they have not mistaken lack of competition for opportunity. Challenging indications like sepsis or stomach cancer may have few therapeutic options, but they have also lost investors significant money in the past and so are likely to require particularly strong *in vivo* data.

Industry learns more from its failures than successes and, as a non-publishing culture the only way for academics to access that knowledge is to take advantage of corporate willingness to share relevant expertise.

Constructing a killer pitch

For the academic entrepreneur who has avoided these pitfalls, there are additional components that differentiate an acceptable pitch from a killer one. The basic essentials are solid intellectual property protection, commercial application for the technology and stellar scientific know-how in the team. Notably, experience in running a startup company is not ranked highly among corporate venture capitalists because they can, and do, hire management expertise as needed. In fact, the feeling is that such experience is not generally abundant among academics, as entrepreneurship is viewed as a one-way process—you do not often see successful

CEOs moving back into academia. A planned exit strategy is also not high on the CVC wish list, with the opinion being offered by one company that they consider exit strategies based on initial public offerings as essentially obsolete today, although there is evidence that this trend may now be reversing.

By far the biggest differentiating factor highlighted by our corporate venture capitalists was confidence in the new working relationship. Corporate venture capitalists look more favorably upon a proposal from an academic team with whom they have previously collaborated, and a record of collabo-

rating with another industry partner is also considered positive, assuming the references check out. This emphasis is possibly motivated by the somewhat eccentric personality traits associated with academics. As one CVC director put it, “Some academics have egos the size of a barn, and some, including Nobel Prize winners with whom I have worked, are simply a joy to work with.” The industry partner also needs confidence in the relationships among team members, particularly with academics who are new to entrepreneurship. This inexperience is significantly offset by the presence of seasoned entrepreneurs on

Figure 2 Milestones that trigger the initiation of a spin-out venture. Industry entrepreneurs demonstrate more targeted views than academic scientists on which translational research milestones should trigger the spin-out discussion.

the team, so including such mentors in the pitch offers another positive.

The final crucial aspect for the academic pitch is to understand the different CVC personalities and tailor the presentation appropriately. Corporate interest can be tightly focused on one area (on lung cancer, for instance, but not pancreatic cancer) because that is the primary indication for the parent company. Others take a more agnostic approach and actively look to establish new areas of science for the parent company. For academics seeking funding, doing the required homework to know which personality most fits their discovery is essential because although there is a willingness to share expertise, there is resistance to wasting time. Discussions that are well informed and targeted can yield excellent results and may entice multiple corporate partners with complementary interests. “We can also bring other companies.... In virtually any of the main pharma VC arms, we have friends,” said Ed Torres, managing director of Lilly Ventures.

Fostering strategic partnerships

These findings raise the question: how can we foster early stage collaborations with industry to support future academic entrepreneurship? A needs analysis of University of Cambridge faculty demonstrated that senior academics with existing industry ties often have a history of successfully closing deals and hence do not need support, whereas scientists new to entrepreneurship lack such networks and are more likely to benefit from help initiating and driving the process. Therefore, when a university is developing a strategy to increase academic entrepreneurship, targeting faculty new to the commercialization of scientific research offers a higher return on investment. The major barrier for such faculty is risk mitigation, as summed up by one budding academic entrepreneur: “As far as industry collaboration goes, we are very native. We don’t know how to start it, what is involved or if we have to sign our children over.” To truly accelerate academic entrepreneurship, this must be addressed (**Box 1**).

As our test case, we took a discovery—a drug designed to mask compounds with a lipophilic or hydrophilic polymer to minimize degradation in the body—and submitted it through the website of 12 global pharmaceutical companies. One month later our success rate for this process was a disappointing 0%. We then tried an alternative strategy, whereby we actively identified key industry personnel who had both the scientific chops to understand the technology and were senior enough

Box 1 Early stage risk mitigation

The pitch is the final value proposition, but there are many early stages in which a nascent discovery, albeit without current marketable value, can be nurtured toward future venture potential. The corporate engines are primed for commercialization, and corporate venture capitalists we spoke with repeatedly stressed a willingness to work with academics in driving the chemistry of early drug discovery more efficiently toward *in vivo* data and venture creation. Even lead identification is not always essential for pre-venture collaborations, for which *in vivo* target validation in a knockout model can be enough to warrant seed discussions. Exploiting such opportunities involves more than simply developing streamlined processes, however; it requires engaging the academic science community, and this involves addressing risk mitigation. Faculty overwhelmingly support the principle of translating academic discoveries onto the marketplace, but some very public failures of partnerships between industry and academia have raised concerns about the time commitment and trust involved in partnering with the very different industry culture. To determine how much of a barrier this cultural disparity poses, we interviewed 13 university entrepreneurs, with experience of up to 6 spin-out ventures apiece, to assess their opinions of industry partners.

In every case the industry collaboration was considered beneficial. “This type of commercial interaction is now essential for many types of medical research,” said Richard Sandford, Wellcome Trust senior fellow in clinical research in the department of medical genetics.

Moreover, industry partners were highlighted as a positive factor in attracting outside investment to academic spin-outs. “They have acted in the best interests of the company and helped bring new investors on board,” said Shaun Fitzgerald, co-founder and CEO of Breathing Buildings.

In terms of confidentiality, interactions were generally carried out under a nondisclosure agreement (NDA), and none of our investigators reported a breach of trust from a corporate partner or had heard of such a case with colleagues. The pharmaceutical industry, in contrast to the software industry, is built on the respect of intellectual assets, and the use of NDAs appears to be efficient and powerful. Chris Lowe, director of the Institute of Biotechnology at the University of Cambridge, summarized the faculty experience when he said, “I have no problem working with NDAs,” adding that “for close industrial colleagues, I won’t even use an NDA.” Industry scientists are similarly compliant: “I would consider [an NDA] watertight. Once such a commitment has been made by all parties, there is intellectual property protection in place,” said Chris Chamberlain, global head of medical genetics at Roche.

to hold a decision-making post.

This was no trivial task. The pharmaceutical industry takes its employee security very seriously, and direct contact information is rarely provided publicly. As such, finding these ‘industry angel’ contacts represents a real challenge, requiring a combination of in-depth scientific knowledge (to understand the technology enough to know whose desk it should land on) and an extensive industry R&D contact network (to actually get the technology onto that desk). An obvious concern with such a personal approach is that it might alienate potential collaborators by seeming intrusive, but instead the industry contacts were appreciative of the effort we had made to identify the right individual within their large and complex organization. “This is a good example of how something will reach the right person,” said Robert Pinnock, director of licensing and external research for Merck in Europe.

This approach is much more complicated

and significantly more time-consuming, but the contrast is astounding. Our hit rate went from 0% to 100% for initial feedback and consideration, and the technology made it to the review boards of 7 of the 12 pharmaceutical companies.

We would be remiss not to include a small note here about the unexpected benefits of our highly specialized scientific ‘dating service’. Once the initial contacts had been established, several companies expressed interest in pursuing additional collaborations with our scientists. Moreover, they were willing to undertake active, second-generation introductions to ensure that good ideas were not lost. “If it is not of interest to us, we can suggest, ‘Have you thought about so-and-so’—we are very well plugged into the industrial network,” said Chris Chamberlain, global head of medical genetics at Roche. In addition to financial backing and business acumen, industry experts have a lot to offer in terms of basic scientific expertise and cutting-edge

resources, areas in which they are keen to engage. “Working with academics is pretty much my job description, and we very much welcome them.... It is not a one-way process as they also recognize that we have a great deal of intellectual knowledge within GSK,” says Malcolm Skingle, director, academic liaison at GlaxoSmithKline.

Conclusions

Fostering industry partnerships to drive academic entrepreneurship in the current, extremely competitive funding environment requires a scientifically driven approach. Research universities are increasingly looking to alternative bodies for funding sources and, as a result, the pharmaceutical industry has become inundated with investment opportunities. To differentiate their venture pitch, universities must build a strong business case to communicate where a discovery fits in the scientific portfolio of a potential industry partner. CVC alone will not address the academic valley of death, but industry’s

combination of funding and commercial expertise offers an orthogonal value add to academic excellence.

At a time when the industry is reducing its own footprint (and personnel) at an alarming rate, it falls to the university to provide a compelling case for channeling resources into an academic proposition.

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Mary Tanner is senior managing director at Burrill Securities. She was formerly senior managing director at Lehman Brothers and managing director at Peter J. Solomon; her work on countless deals includes biotech’s second-ever initial public offering and the Roche-Genentech merger. In her conversation with *Nature Biotechnology*, Tanner details the Amgen-Immunex buyout, defines ‘wildcatting’ and suggests the years in which children most need a parent around the house. <http://www.nature.com/nbt/podcast/index.html>.