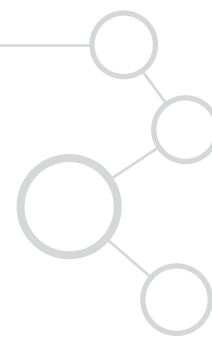


Uniting Science and Business: The Challenges for Biotech Start-ups



By Fiona Brown, Public Relations Consultant

Fiona Brown has a background in public relations consultancy in the pharmaceutical, biotechnology and medical device industries. As a consultant, Fiona supports companies in developing their communications strategies for funding rounds, flotations, market positioning and the development of partnerships with industry majors. She also writes widely on biotechnology, pharmaceuticals and health care. Fiona has a BA from London University and is a member of the Institute of Public Relations and the Chartered Institute of Marketing.

Money is something every biotech start-up needs and will continue to need in ever-increasing amounts. Robust science, a vision and resilience will get you started but at some point you need money, whether from revenue or investment, to progress your science and grow your company. Along the way there are challenges that face any growing company, some specific to biotech, some not.

DEALING WITH THE UNEXPECTED

A young company will encounter a variety of business hurdles. Not uncommonly, companies set out with one vision but then have to re-invent themselves to deal with the unexpected. Nottingham-based biotech Scancell, for example, was originally set up to develop a blood test for Down's Syndrome that would replace the more invasive amniocentesis procedure. Alas, the test did not produce a clear cut answer, but there was a silver lining. The antibody in the test was in fact interacting with epidermal growth factor (EGF) which at the time was newly implicated in cancer. So Scancell's co-founder, Professor Lindy Durrant, adapted and turned Scancell into an oncology company.

While the original science behind a company can disappear, so can its partners. Jeff Errington spent 10 years working on a new class of antibiotics when he decided to start Prolysis. The company was originally conceived as a drug discovery biotech and also offered fee-for-service contract development to provide a revenue stream. As part of this scheme, Prolysis went into a commercially complementary partnership with a larger biotech which stumped up £2 million of seed money. Unfortunately, the partner went out of business and although Prolysis was left with the science and the company infrastructure, it had lost its partner and main investor. This was the late 1990s, when several companies were looking at solutions to the antibiotic conundrum and a number of big pharma companies were merging. "Almost overnight", says Errington, "our pharmaceutical customer base halved and then went into purdah to re-organise. We had to re-finance fast".

CAN YOU PUT IT IN A BOX?

For science to qualify as 'robust' it needs to be capable of moving quickly from 'bench to box'. Research targets must have the ability to become commercial products. For example, Paris-based IntegraGen is developing diagnostics for diseases such as mature onset diabetes in the young – MODY. In France, all children are tested for early onset Type I diabetes, but currently no other test exists for MODY, an increasingly prevalent version of the disease. IntegraGen started out in business with a technology for finding drug targets and an ambition to be a drug development company. As its current CEO, pharma veteran Jan Mous says: "Targets are not a starting point for a trading company". He has helped the company move to the point where its first diagnostic has FDA approval and it is building a sales and marketing infrastructure.

THE PEOPLE GAME

To bring products through the market approval process requires expert business managers and scientists. A big pharma commercial partner at the clinical trial stage, or when the product is ready to be marketed and distributed, provides the commercial expertise not all founding scientists have.

Small companies cannot always afford a fully fledged management team. Trigen's strategy was to stay virtual and validate its science before forming a company with all the attendant costs. Guided by Dr Sanjay Kakkar, 2004 winner of London Biotechnology Network's Young Entrepreneur of the

Year, the research stayed within the safe environment of the Thrombosis Research Institute (TRI) project run by King's College, London, and the Royal Brompton Hospital. They had set up a drug discovery unit based on identification of the deep vein thrombosis characteristics pioneered in the 1970s. From these studies they developed the anti-coagulant heparin and have now developed a low molecular weight version.

Trigen stayed virtual for five years but did source big pharma experts to guide its project and introduce a commercial eye. "Trigen built up an asset without a company rather than set up a company and then try to build up an asset", says Dr Kakkar. Would they have done things differently? "We could have gone faster with specialised finance. But would we have got the big pharma team without the promising science?" he commented.

Founding scientists find the interim manager route can work well. Prolysis brought in a temporary CEO to help put the urgent funding together when its partner collapsed and the mergers caused the pharma customer base to contract. After a successful round, the challenge was then to find a permanent replacement. A new CEO was appointed within a year and is now driving the company forward.

Not surprisingly, the start-ups that are the envy of their peers are the spin-outs from larger concerns that arrive with a ready-made management team, key scientists and a product pipeline. PowderMed had that luxury, because four key people came over from the larger company, PowderJect, to join CEO Clive Dix. "It was fantastic. They were all totally engaged. People said you will fall out, you won't all survive. But it didn't happen. We debated and argued, but managed to come through".

THE BLOCKBUSTER CLIMATE

Raising money is the big challenge for new biotechs and the biotech business model has changed radically in the last five years. Before the dot.com bubble burst, it was possible for a clever scientist with a good idea to set up a company, attract venture funding and come back for more. Companies could float once a product got to proof-of-concept stage. The venture capitalists exited with the return on their investment, and were able fund the next round of newcomers. IPO valuations were high and private investors happily piled in hoping to back a blockbuster drug, but then there were the failures, the sector lost its shine, and subsequently its investor appeal.

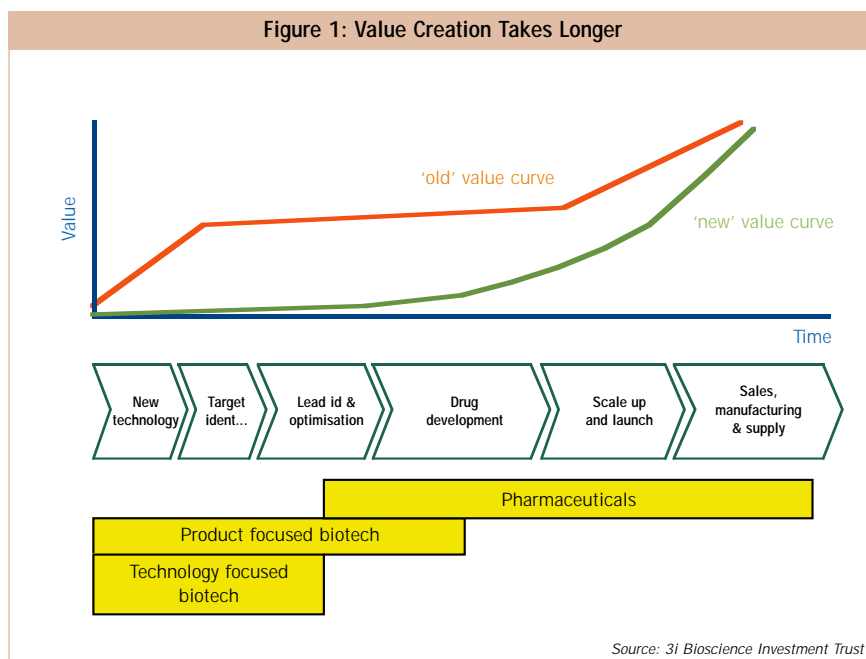
A NEW MODEL

Now in 2004 things are different. Where once new companies raised their seed money through a mix of grants, venture

capitalists and business angels, now business angels are increasingly the key source. When more substantial funds are needed, especially to take drugs into the clinic, VCs are still the main source of finance, but they have become very tough nuts to crack. VCs want to see signs of profit, even products developed as far as Phase III, and companies claim that VCs drive down valuations to get a cheaper investment. One reason for this is that without the one-time available exit route through flotation, a large proportion of VC funds are needed to support companies that were once the start-ups.

The challenge for biotechs in this new money world is to not only get initial funding, but also to replenish it before the coffers run dry. To do this, they must demonstrate that they are passing ever tougher milestones and adding value to the company. As Alison Thorp of 3i Bioscience Investment Trust says: "A company's value does not start its significant uplift until it has products on the market. In the past, the value for drug developers, for example, started to lift appreciably at the earlier manufacturing scale-up stage, before launch" (see Figure 1).

In the new funding environment, today's entrepreneurial CEOs need to be more imaginative. Trigen's Dr Sanjay Kakkar managed to get seed money for early research in an academic unit from investors who already had a donor relationship with the hospitals that started the unit. When it came to finding VC money, Dr Kakkar brought in Robertson Stevens as advisers to target funds in Europe and the States. The consultants took a focused approach and concentrated on finding a VC who would share the company's vision. They found HealthCap of Sweden and the Series A round allowed Trigen to go from virtual to integrated and acquire the TRI project group and equipment. While considering further financing, Trigen also sees M&A as an attractive route with its additional benefits of achieving critical mass and building a broader discovery engine.



THE DILUTION FACTOR

Another hurdle that companies often have to overcome in the funding process is switching lead investors, as it's at this point that the wrangling can start over the valuation of the company. The first investor may not want to take on greater exposure to risk, but at the same time still wants to see its smaller equity percentage as part of a more valuable investment. Furthermore, the biotech company may have already sacrificed half its equity and will not want to lose more of the company to new investors.

Scancell's CEO, Mike Capaldi, also warns that business angels could lose interest in the sector if valuations are driven down when VCs enter the fray, leaving angels little return on their original investment. "They put their money in at what you said the company was worth and now you're raising money at a fifth of the price. It needs a new look at preference shares and anti-dilution clauses".

THE FINANCIAL TREADMILL

After the first funding round, raising additional money can become something of a treadmill for the CEO and senior executives. "It's the short-termism of the process that's the issue," says Capaldi, "as you finish one round you have to start the process all over again. With nothing ready for the clinic for say at least another 18 months and partnering unlikely before Phase II, it's all rather difficult. You need at least two years' worth of money to make some progress and it may be unreasonable to expect a longer leash," he concedes. "But it takes nine months to raise money, only leaving a few months before you're out on the road again. In January you say to VCs 'we are expecting to achieve X & Y by December' and they say, 'OK, we'll look at you then'".

WE LIKE PRODUCTS

In the high risk area of pharmaceutical research, where a company can be too dependent on VC money, there is the threat of a cash crisis before milestones are reached. A better bet for VCs is a company with products. Oxford Immunotec, a diagnostics business, has adopted the more popular business model of low technology, low risk. Its platform technology, based on a blood test to detect a T-cell mediated response to infection, has potential across a broad range of conditions including cancer, allergy, HIV and other immune diseases. It has managed to move from 'bench to box' in a rapid 14 months, with the first commercialised test launched in August this year. The reason for this speed is the decision to hold back on building a company in favour of accumulating literature references. "Publishing widely has been the best pre-marketing we could have had," says CEO Peter Wrighton Smith, "now we can look for more funding to bring our other diagnostic tests through to market".

COMPETITION AND COMMUNICATION

Biotech is an ideas business and can be inspiring not only to scientists but also to the idea-hungry world of big pharma and, ultimately, the investor. However, science is a fickle friend because its secrets are constantly unfolding. Just as one approach looks to be the winner, another idea can suddenly appear in the outside lane and overtake. A disease target can be discovered but it may not have druggable potential. A drug delivery vehicle can look like a universal solution but then turn out to work only in a particular application.

New products are the lifeblood of all manufacturing industries. Biotech, unlike big pharma, are forced to conduct their drug development in the public eye in order to attract support, both financial and commercial. Managing the news flow through the ups and downs is a constant communications challenge.

Newly-formed PowderMed is a case in point. The company was established in 2004 with the original PowderJect needle-free vaccine delivery technology. PowderJect, as the name implies, was founded on the promise of this technology, but it soon discovered that 'one delivery suits all' wasn't the case, so it brought in traditional prophylactic vaccines. "The other things, such as the injection, were a distraction," says Clive Dix, former CSO at PowderJect, who left when Chiron bought the company. He knew that the potential for the technology lay with cure not prevention, in other words, with therapeutic vaccines not prophylactics. He submitted a proposal to Chiron and PowderMed was born. "Outsiders, however didn't quite understand the logic of what had been spun out as PowderMed," he says. "We had to educate these audiences. PowderJect's high profile helped us through the door, but the messages had to be changed. Things had moved on since the promise of a painless, needle-free world. It was not going to revolutionise everything. But 'DNA on gold', which we have at PowderMed, will be good for therapeutic vaccines. People eventually understood and could see it was a sensible business."

CONCLUSION

Looking at the challenges new biotechnology companies face today, especially with regard to funding, one wonders if the process will ever get easier. From the perspective of a start-up CEO, Ian Charles, Professor of Molecular Biology at the Wolfson Institute, UCL and former CSO of Arrow Therapeutics: "the challenge is how to incentivise the early entrepreneurs in the universities who are critical to the development of new products and ideas. Cutting the equity cake fairly, providing enough funds and at the same time motivating and nurturing the best to provide the necessary return remains the challenge, whatever business and financing models are in vogue". ♦

*The author can be contacted at
f.brown@lineone.net*