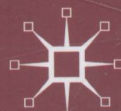


Venture Capital and the European Biotechnology Industry



William Bains



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Venture Capital and the European Biotechnology Industry

Also by William Bains

Biotechnology from A to Z

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1

Genes and Money in Europe: Why Did It Fail?

This book is slightly unusual. Most business books are about how to run a successful business. This one aims to be a detailed, fact-based primer on how to fail in one of the world's most exciting and fast-moving industrial sector – biotechnology.

The biotechnology industry is replete with good-news stories, icons of wealth creation, morale-boosting tales of corporate heroics. Many reviews of 'how to make a successful biotech company' explicitly ignore the example of failures, which is rather like making a film called 'how to live forever' in a graveyard.¹ There are many hard-working, expert and dedicated people working in biotechnology, in science, in venture capital (VC) and in the companies which bring them together. And they have created a few outstanding successes. But any new business endeavour is an experiment. All Western economies are constantly trying out new types of business, creating what Metcalfe calls 'restless capitalism' [1] where knowledge of past events drives not just new products but new ways of doing business and finance, and the knowledge thereby gained drives yet more innovation. The biotechnology industry was such an experiment, and by the measures I present here, the late twentieth century European biotechnology experiment failed. This is the overwhelming reality of the industry in Europe, and especially in the UK, recounted by nearly every biotech entrepreneur I have talked to in two decades of doing business in biotech. On the European side of the Atlantic, 'biotechnology' is a byword for opportunities wasted, careers destroyed and private lives ruined, of waste of government and personal resources, lost wealth and opportunity for European economies and of throwing away biomedical opportunities that could be of real, lasting value to us all.

None of us are getting younger, fitter or healthier. Throwing away the opportunity to do something about that, for short-term financial gain,

is not a great idea. Throwing it away in order to make a loss seems positively absurd. So I have spent five years researching why this is happening, and this book is the result.

It is the contention of this book that there are three principle contributors to this failure: the management, the government and the investors. The manifold failings of greedy entrepreneurs, egomaniac founding technologists, power-crazed CEOs and academics completely divorced from reality, are covered in many other places. This book does not wish to claim that these are not real problems: a business must be built on good commerce, good management and a practical growth strategy, not just 'great science'. We will cover how realistic the views of company creators and management are in Chapter 7. Less often critiqued is government policy across Europe. To summarise policy to the point of parody, it has been this: some enormously successful US biotech companies started as start-up companies based on cutting edge university research, so if we are to stimulate the creation of spin-out companies based on University research then they will become huge and successful biotech companies. The flaws in this Cargo Cult Economics are starting to be understood, but the damaging knock-on effects are generally not, so I will analyse this cause of failure in Chapter 12.

But these factors would not have resulted in an industry that is a Bonsai² imitation of its grown-up US counterpart if not for the influence and effect of the most powerful force in the economics of biotechnology. That is, the private investment industry, called (rather inaccurately in Europe) VC.

The assumption built into most analysis of VC in biotechnology is that it is a 'good thing'. This image of VC is rather different from the experience of many companies and entrepreneurs in European biotechnology. VC is often, and loudly criticised by entrepreneurs. Entrepreneurs often feel that VC feeds on their efforts and returns nothing, a feeling reflected in the well-known joke that 'VC' stands not for 'VC' but 'Vulture Capital'. (But vultures are useful animals, recycling the remains of carcasses that have already fed the lions or wolves. I have long thought that the feelings of most entrepreneurs are better captured by the phrase 'Vampire Capital'. The vampire stalks a beautiful, defenceless young thing with 50 years of success and happiness ahead of her, seduces her with illusions and then sucks the life out of her³) But this type of abuse, even though derived from deep experience of the problems, is usually written off as sour grapes from entrepreneurs whose dreams of wealth and prestige have not been realised. This literature, large and largely web-based, is not a terribly reliable source of statistical evidence for economics. To counter

it, VCs and their spokes-organizations such as EVCA⁴ and BIA⁵ provide case studies of how VCs have rescued ailing companies from the grasp of their incompetent founders and turned them into commercial and technical successes – again, we should view such anecdotal data as suspect.

This book, therefore, aims to provide a detailed, factual analysis of the effect that the present model of investment has had on high-tech start-up companies in Europe, and some analysis of the mechanisms (and hence reasons) behind it. It is the factual backup for what many entrepreneurial scientists and businessmen in the biotechnology community have learned as unproven but obvious over the last decade, and as such I hope it is some use to them. I hope that many readers, even if they do not agree with my conclusions, can use this source of factual data about the industry and its investors for their own purposes.

I have not tried to propose what one entrepreneur colourfully called ‘A universal theory of VC suckage’ [2]. I do not believe there is one. Rather, investor and entrepreneur activity, driven by a range of *ad hoc* reasons, and the VC business model which propels these which I describe in Chapter 11, is a rational response to the economic environment in which VC management groups find themselves. There is no plot to do down entrepreneurs, and make sure that innovative drugs never reach the market – it is a mistake to see incompetence as conspiracy. Nor do I claim that ‘sorting out’ VC would make European biotech rise, phoenix-like to out-compete the Americas. This is an analysis of one aspect only, and VC apologists remain free to dismiss what I present here as one small aspect of the problem, possibly true but of no significance. That is their prerogative.

I have also not tried to tie this to formal economic or business theory, although I have referenced some of it where it is relevant. There is a mass of literature on what *should* happen in high-tech company finance, based on logical and mathematically sound economic arguments, (which usually assume that people are informed, rational agents, which undermines their arguments from the start). There is a mass of literature (mostly PR material for various interest groups) on what people *would like* to happen. This book, however, is based on data of what actually *did* happen. There is no point, therefore, in contesting my assumptions: my assumptions are *what actually happened*. You may choose to contest my choice of facts and my conclusions. But saying ‘that just is not true so’ will not refute the argument.

Having said that this is a book based on fact and statistics, I do not pretend that I started out with no idea of what the conclusion would be. It is clear that VC practices in Europe have at very least been ineffective

at creating successful companies, at worst been positively toxic to entrepreneurship and company creation. What I have tried to do here is demonstrate that the intuitive feeling that this is so, felt by many entrepreneurs, managers, personal investors and not a few VCs, is backed by the facts. Since the start of 2008, the credit crunch, and the flight of VC from funding biotech of any sort in Europe, such views have become more common, and indeed some will regard this book as a post-mortem of a business model already dead. But the same things were said in 2002, and VC survived, and indeed flourished in its own way. The VC model is not dead – at most, it is hibernating through our current economic winter. This will be an enduring issue, and it is my hope that this book helps address it.

Many people have helped me in writing this book, and in the research over the last few years which I summarise here. My sincere thanks to them all. Quite a few wanted to stay anonymous, for reasons that will become obvious, so I will not name names. Several of them advised me not to write it at all if I ever want to work in a VC-backed industry again. Ladies and gentlemen, I will take that risk, again for reasons that I think this book will make clear. My thanks also to the staff and students of the Cambridge University MPhil in Bioscience Enterprise course, to the good folk at Palgrave Macmillan for taking a risk with me, and steering me clear of some even greater ones, and to you, gentle reader, for reading at least this far. Now read on!

2

The Biotechnology Industry and Venture Capital

This is not a book about the *technology* of biotechnology, but about the *business* of biotechnology. The latter is dependent on the former, but can be described without ever explaining what a gene is.¹ I will try to keep it that way.

The biotechnology industry takes novel life science discoveries or technologies and turns them into products [3]. It is one of the highest-profile science-based industries, with over 4000 companies, \$63 billion in revenues and \$20 billion in R&D investment worldwide, with a quarter of those companies and three-quarters of the revenue in the US [7]. The highest profile of such companies are the 'biotech start-ups', new companies created to commercialise specific pieces of technology, and these are often considered typical of high-tech entrepreneurship as a whole. These companies are the subject of this book.

The modern biotechnology industry started in the mid-1970s, when a number of pioneers realised that the new advances in explaining how living things worked in terms of molecules could be put to practical use. The initial applications were in the US, with the creation of companies such as Cetus, Chiron and Genentech. But Europe was not far behind, with the foundation of Celltech and Biogen and the growth of companies such as Serono (founded in 1906 but revitalised as a modern biotech company when it moved to Geneva in 1977 and launched its growth hormone product). In the US and Europe at this time several larger companies, notably Kabi, Eli Lilly and Novo, were also active in building a biotechnology research infrastructure.

However, what distinguished the new industry from Eli Lilly, Novo and Serono was the new companies created explicitly to exploit the application of the 'new biology'. It was the creation of an entity called a 'biotechnology company' in the late 1970s in the US and early 1980s in

Europe that galvanised scientist and government alike. Scientists saw a way of sidestepping the size and stratification of major corporations and the University system and turning *their* science into money and fame. Governments saw a way of creating a whole new, clean, knowledge-driven industry from their investment in further education and basic research. And investors saw products that would revolutionise the world and make them rich in the process. In 1980, when Genentech floated and its stock price doubled in the same day, this seemed an industry that could not fail. Move over Microsoft, the genes were coming.

The only drawback, and the major difference between Microsoft in 1973 and Cetus in 1973, were that biotechnology required substantial investment to produce a product [8]. While a teenager could (in 1973) produce a commercial computer program in his bedroom, biotechnology took laboratories, PhD trained scientists and many years: Amgen took two years just to isolate the gene for erythropoietin (EPO), its initial best-selling product, which had to be followed by five more years of scale-up, production, trials in animals and humans and then approval by the FDA (US Food and Drug Administration) before they could generate revenue: by today's tightened regulatory standards, that is considered exceptionally fast. So the new companies were dependent from the outset on people to provide investment capital to support their very expensive R&D efforts.

Of course, this only applies to companies that plan to do R&D. From before 1980 there was an assumption in the mind of scientists, investors and journalists that 'a biotechnology company' was one doing research to create new products (and we will later examine why that might be). But it is quite possible to set up a 'biotechnology' company that just sells the product of existing technology, and if this is not to a highly regulated market such as health care, then they can do that almost immediately. So there have been three types of biotechnology companies. Small 'garage biotechnology start-ups' did not attract major market attention until, like Invitrogen, they floated on the basis of being a profitable business. These companies are often characterised as 'lifestyle businesses' set up to generate cash to sustain what their founders are good at. It is a business model sneered at by VC, but it is capable of building multinational corporations (Microsoft and Google started as teenage lifestyle businesses). A textbook example in biotech might be Bangs Laboratories, founded by Leigh and Sonia Bangs in 1988, literally in their garage, to produce specialised reagents for research scientists, or UK companies such as Oxford Ancestors or AbCam (the latter floated in 2005). If they receive investment at all, it is from private investors – 'Business Angels'.

Exact figures on Angel investments are hard to come by, but it is estimated that even in the UK, where there is a relative lack of wealthy individuals and a culture that runs counter to private risk investment, Angels probably invest as much as VC and, because they invest in smaller companies, actually support eight times as many start-ups [9]. We will address the relationship between VCs and Angels at the end of the book.

In fact, many of today's European success stories started this way. Cambridge Antibody Technology had no venture investment – it was funded by research programme and corporate investment from its partners, notably Peptech. So the second business model, widely ignored but proven to be successful, was the 'big garage' start-up, the company which started with a vision to be a major corporation but which funded itself from non-equity income from the start. The evidence suggests that this is in fact the 'normal' model for company development in Europe, with over 50% of the publicly quoted UK biotechnology companies in 2006 having never received any VC investment at all.

However, the most widely recognised third business model for creating and building a biotech company is to start with some science and an idea of the product it can be turned into, gather investment to realise that product, spend years researching it and only then sell the product to generate revenue. The usual product is a new drug, for a variety of (partly fallacious) reasons that I will discuss later. Such ventures are enormously risky, with drug discovery and development typically taking 12 years and costing \$350 million even if successful [10]. This type of technical development costs too much to be sustained by personal investment, so the biotechnology industry has relied on investment from institutional investors who are able to put \$10 million or more into a company at each investment stage [11]. This is the role of the VC group.

VC groups in the US are institutional investors who specialise in high-risk, high-return investments where their expertise and involvement in their investee companies can add value that others cannot see or realise [12]. Banks and pension funds will not commit funds to a project based on science that they do not understand with a 50% chance of complete failure, and only a 2% chance of major success. VC can, and sometimes does.

In addition, companies requiring smaller amounts of investment might turn to VC because it is the only source of investment that they know. Many entrepreneurs comment that closing an investment deal with a Business Angel is not hard (in the sense of being excessively drawn-out or punitively dilutive), but because Angels do not generally advertise their wealth, finding them in the first place is the major barrier [13]. Indeed,

Angels often have a 'passion for secrecy', and so entrepreneurs do not realise the volumes of cash available [14]. In the 1990s, many biotechnology companies may have gone to VC simply through ignorance that other alternatives existed. The rise of Angel Networks post 2000 is changing this landscape.

Because of this close link between VC and biotech, the industry is often seen as being almost symbiotic with VC in the US and in Europe [15–17]. Kenny comments, 'Biotechnology has emerged as an industry largely because of one economic institution: VC.' [18], page 133. Many spin-out companies aim to obtain VC as an integral part of their development.

Although this explanation is only partly correct, as we shall see, it is certainly true that in countries such as Japan, with a very high scientific reputation and output but minimal VC activity, there was little biotechnology industry in the Western sense in the 1980s and 1990s.

I should digress here briefly into the mechanics of VC investment in any company, including biotechnology companies, to make sure the reader is familiar with the processes and jargon that we will be handling later in the book. Readers familiar with the VC investment process may skip ahead to page 9.

Companies wishing to raise funds from investment do so by issuing new shares or 'stock' in the company. This is distinct from existing shareholders selling their shares – in the latter case the shareholders get the cash, the company does not, so that does not help raise funds for the company's activities. So the company creates, or 'issues', new shares to sell to the investor, and the company itself gets cash as a result. The obvious question is how many shares a company must issue to get a specific amount of cash, and that is defined by what fraction of the company those shares represent and what the value of the company as a whole is. The former is a minor technical matter, but the latter is critical, and is the issue of *valuation* of the company.

A company's valuation depends on its current assets and likely future assets, including revenue (an important point we will return to in Chapter 8). Obviously, these will change with time. Discovering what a company's probable future asset value is likely to be is hard enough for a company with a ten-year trading record. When the company's sole present asset is a research programme and some patents, working out its value in five years' time is almost impossible. So it takes a lot of work to evaluate a company's value, and this is not something the VC wishes to do continuously. For this reason, and because of the complexity of the investment mechanisms (some of which we will discuss further