1
Introduction

1.1
Development of the Private Equity and Venture Capital Market

1.1.1
Definition

Private equity is an asset class consisting of many forms of high-risk and high-return equity investments into companies not traded on a public stock exchange. Private equity deals are generally thought of as a long-term investment (International Financial Services London, 2006). Investments typically involve a transformational, value-added, active management strategy helping start-ups improving their fundamental business practices. By that means, private equity may be considered as one of the most potent forces enhancing economy-wide improvements in corporate productivity. Private equity firms pursue one major goal – to search for companies with the potential for growth and to put in place the capital, talent, and strategy required to permanently strengthen the company and raise its value. Private equity is often subsumed under the umbrella of 'alternative investments,' complementing the stock and bond portfolios traditionally used by investors (European Venture Capital Association, 2007a). Private equity can further be subdivided into venture capital, mezzanine capital, buy-outs, and turnarounds/distress (Metrick, 2007).

Venture capital, often also referred to as 'smart money' because it comes in a combination of know-how and a network of experts, by definition refers to private equity investments made for the launch, early development, or expansion of a business. Venture capital focuses on new entrepreneurial undertakings rather than on mature businesses (European Venture Capital Association, 2007a). It represents only a small proportion of the overall private equity market. Venture capitalists act as financial intermediaries, who take the investors' capital and invest it directly in portfolio companies (Metrick, 2007). Investments can be classified into seed-stage, start-up, expansion-stage, and replacement capital. Seed-stage capital is financing provided to research, assess, and develop an initial concept before a business has reached the start-up phase. Start-up stage capital is financing for product development and initial marketing, expansion-stage capital is financing for growth of a

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company which is close to break-even or trading profitably, and replacement capital is used to purchase shares from another investor or to reduce gearing via the refinancing of debt (International Financial Services London, 2006). A special form of venture capital is corporate venture capital, a term used to describe the investment of corporate funds directly in external start-up companies, which are then free to operate independently and to make autonomous investment decisions. These corporate venture capital firms will often be led by strategic objectives other than financial results and will have neither dedicated capital nor an expectation that capital will be returned within a certain time frame (Metrick, 2007). Examples of such corporate venture capital funds in biotech are the Novartis Venture Funds and the GlaxoSmithKline SR–One Fund.

Mezzanine money has two different meanings in the private equity industry. The first refers to a form of late-stage venture capital, with financing typically occurring in the form of subordinated debt and some additional equity participation in the form of options to buy common stock. The second meaning of mezzanine first arose in the mid-1980s, when investors started to use the same capital structure, i.e., subordinated debt with some equity participation, to establish yet another layer of debt financing for highly leveraged buy-out transactions. Today, most private equity firms offering mezzanine capital practice the latter type of investing (Metrick, 2007).

Buy-outs, which occur when a private equity investment firm gains control of a majority of the company's equity through the use of debt, are by far the largest private equity segment. These are typically investments in more mature companies. The acquisition normally entails a change of ownership (International Financial Services London, 2006). In large buy-outs, the investors put up the equity stake, today usually between 20% and 40% of the total purchase price, and borrow the rest from public markets, banks, or mezzanine investors – hence the term leveraged buy-outs (LBO; Metrick, 2007).

Finally, turnarounds are investments into a distressed company or a company where value can be unlocked as a result of a one-time opportunity, such as changing industry trends or government regulations (Metrick, 2007).

Private equity funds typically have limited and general partners. The general partners are generally represented by the private equity investors who manage the fund. The limited partners are institutional and individual investors who provide capital. These are limited in the sense that their liability only extends to the capital that they contribute (Lerner and Gompers, 2001). The most common limited partners are institutional investors, such as pension funds, banks, insurance companies, or endowments. Each fund raised by a private equity company is invested in a number of firms with a five- to ten-year horizon. When a fund is ended, its cash proceedings, coming chiefly from initial public offerings (IPOs) and trade sales, are distributed to investors together with any remaining equity holdings. The number and variety of groups that invest in private equity have expanded substantially to include a wide range of different types of investors. Until two decades ago, the private equity market primarily consisted of wealthy individuals investing in early-stage companies. In recent years, the situation has changed and there are now many institutional investors with long-term commitments (International Financial Services London,

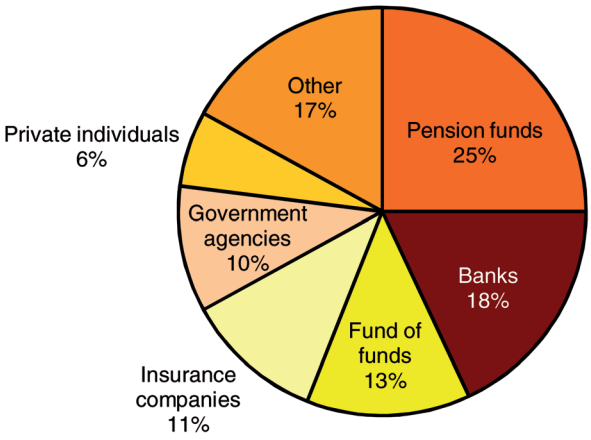

Figure 1.1 Sources of new funds raised in Europe (International Financial Services London, 2006).

2006). The distribution of the different private equity investor types in Europe is shown in Figure 1.1.

Private equity firms generally receive a return on their investments in one of three ways, i.e., an IPO, a trade sale or merger, or recapitalization (as in the form of a management buy-out). An IPO is the first sale of stock by a private company to the public. Such a stock market flotation may be the most spectacular exit, but it is far from being the most widely used, even in stock market booms. For an IPO to be successful, the company first has to invest enormous amounts of time and money into building a pipeline that is likely to attract investors. Furthermore, IPOs are associated not only with substantial one-time direct and indirect costs, but also with ongoing costs and the need to supply information on a regular basis to investors and regulators for publicly traded firms (Ritter, 1998). A stock market flotation should therefore reflect the genuine wish to make the company more dynamic over the long term and to profit from the growth possibilities offered by a stock market. Once the stock is publicly traded, this enhanced liquidity allows the company to raise capital on more favorable terms than if it had to compensate investors for the lack of liquidity associated with privately-held companies (European Venture Capital Association, 2007a). Also, existing shareholders are able to sell their shares in open-market transactions (Ritter, 1998). Overall, a flotation is not an end in itself, but the beginning of a long development process (European Venture Capital Association, 2007a).

Trade sales are a very popular alternative route for a divestment. A trade sale of a privately held company equity, also referred to as mergers and acquisitions (M&A), is the sale of company shares to industrial investors. Large and small companies often complement each other, and an alliance between them will not only serve to round off their portfolios, it will also guarantee a strategic advantage to at least one of the companies teaming up. This is why buyers are often willing to pay a premium to acquire a complementary business (European Venture Capital Association, 2007a). Although the terms 'merger' and 'acquisition' are often used as though they were synonymous, they do mean slightly different things. When one company takes over

another and clearly establishes itself as the new owner, the purchase is called an acquisition. From a legal point of view, the target company ceases to exist, the buyer 'swallows' the business, and the buyer's stock continues to be traded. In the pure sense of the term, a merger happens when two firms, often of about the same size, agree to go forward as a single new company rather than remain separately owned and operated. Both companies' stocks are surrendered, and new company stock is issued in its place. In practice, however, actual mergers of equals do not happen too often. Usually, one company buys another and, as part of the deal's terms, simply allows the acquired firm to proclaim that the action is a merger of equals, even if it is technically an acquisition.

Recapitalizations are based on a company incurring significant additional debt by repurchasing stocks through a buyback program or by distributing a large dividend among its current shareholders. This causes the share price to soar, making the company a less attractive takeover target. Recapitalizations are mostly used to fend off a hostile acquisition. The repurchase of a company by its management team, the management buy-out (MBO), is becoming more and more successful as an exit strategy. It is a highly attractive option for both the investment manager and the company's management team, provided that the company can guarantee regular cash flows and mobilize sufficient loans (European Venture Capital Association, 2007a).

1.1.2 Historical Background

The seeds of the private equity industry were planted in 1946, when Harvard professor Georges Doriot created American Research and Development (ARD) together with Karl Compton, then president of the Massachusetts Institute of Technology, Merrill Griswold, former chairman of the Massachusetts Investors Trusts, and Ralph Flander, then president of the Federal Reserve Bank of Boston. ARD's overall aim was to raise funds from wealthy individuals and college endowments and to invest them in entrepreneurial start-ups in technology-based manufacturing. Its founders believed that by providing management with skills and funding, they could encourage companies to succeed – and in doing so, make a profit themselves (Bottazzi and Da Rin, 2002).

In the 1980s, FedEx and Apple were able to grow because of private equity and venture funding, as were Cisco, Genentech, Microsoft, Avis, Sun Microsystems, and many others (Bottazzi and Da Rin, 2002). Despite these successes, private equity companies came to be regarded with acrimony because of a series of debt-financed leveraged buy-outs (LBOs) of established firms, casting private equity firms as irresponsible corporate raiders and as a threat to the free capitalist structure (Burrough and Helyar, 2003).

LBOs were pioneered by Jerry Kohlberg, Henry Kravis, and George Roberts, who later founded the private equity firm Kohlberg Kravis Roberts (KKR). The idea was to employ aggressive forms of financial engineering to increase shareholder value. For this to work, certain management principles were to be followed, i.e.,

recapitalization of the company to substantially increase debt, a concentration on maximization of after-tax cash flow from operations, the sale of unnecessary assets, and motivation of the management with exceptionally high compensation incentives. After several years of intense management, they would take the improved company public again or sell it to a larger corporation, in this way returning capital and a double-digit return to investors (Smith, 2007).

In the first half of the 1980s, the annual flow of money into venture capital funds increased by a factor of ten, but it steadily declined from 1987 to 1991. Through the 1980s, the rise was even more dramatic for buy-outs, but this too was followed by a precipitous fall at the end of the decade, mostly due to changing fortunes of private equity investments. In the mid-1980s, returns on venture capital funds declined sharply. This fall was triggered by overinvestment in a few industries, such as computer hardware, and by many new and inexperienced venture capitalists entering the scene. A similar decline was seen for buy-out returns in the late 1980s, due largely to the increased competition between transactions. As investors became disappointed with returns, they spent less capital in the industry (Lerner et al., 2005).

The 1990s were characterized by similar patterns on an unprecedented scale. Much of the decade saw dramatic growth and excellent returns in the private equity industry. This recovery was due to the withdrawal of many inexperienced investors, ensuring that the remaining groups were facing less competition for transactions. Moreover, there was a healthy market for IPOs, guaranteeing easier exit for equity investors. Meanwhile, the extent of technological innovation created extraordinary opportunities for venture capitalists. New capital commitments to both venture and buy-out funds increased to record levels by the late 1990s and 2000. Yet, private equity grew at a pace that was too fast to be sustainable. Institutional and individual investors, attracted especially by the high returns of venture funds, flooded unprecedented amounts of money into the industry, often resulting in overchallenged partners, inadequate due diligence, and poor investment decisions (Lerner et al., 2005).

After reaching a peak in 2000, private equity funds fell between 2001 and 2004, mainly due to the slowdown in the global economy and declines in equity markets, particularly in the technology sector. In 2005, market confidence and trading conditions improved again, with US$135 billion of private equity invested globally, up one-fifth on the year 2004. Between 2000 and 2005, buy-outs generated a growing portion of private equity investments, increasing from one-fifth to more than two-thirds. By contrast, the share of venture capital investment fell during this period. Private equity fund raising also reached a peak value of US$232 billion, up three-quarters on 2004. In 2006, according to International Financial Services London, the positive trend continued, with a record amount of US$365 billion of private equity being invested globally and with private equity fund raising amounting to US$335 billion, both marking a significant upswing to the previous year (International Financial Services London, 2007).

Historically, Europe has had to grapple with more impediments to private equity than the US, not least because of tougher labor and bankruptcy laws. However, also in Europe, the ability of private equity investors to restructure, grow, and sell profitably

has, over the past years, generated more and more interest from key players, such as debt providers, pension plans, and public company CEOs (Blaydon and Wainwright, 2007). Between 2000 and 2005, Europe increased its global share of private equity investments from 17% to 43% and raised funds from 17% to 38%. This was largely a result of strong buy-out market activity in Europe. In contrast, private equity activity in North America decreased from 68% to 40%, and raised funds dropped from 69% to 52% (International Financial Services London, 2006). This illustrates that private equity represents an increasingly important source of financing for European growth businesses. More than half of all private equity investments go into small and medium-sized companies with 100 staff or less, with these enterprises representing the main source of new jobs in many economies (Gaspar, 2007). On average, companies financed by private equity develop faster, invest more, and generate more jobs. Private equity firms themselves contribute a lot more than just funding, including hands-on management expertise, counseling, and access to regional and global networks. Without the involvement of private equity firms, many companies would not have been founded, reorganized, or found successive owners or managers (Frommann, 2007).

1.1.3 The Challenges to Private Equity in Europe

However, this does not mean that private equity is not facing challenges. Thus, fundraising in Europe is currently geared towards buy-outs, reducing the volume of available venture capital invested in early-stage development. More importantly, private equity is a boom-and-bust business that is highly sensitive to the whims of economic cycles. The past ten years have seen sharp fluctuations in the capital raised by private equity funds. The consequences of this are two-fold. First, capital availability to support private equity business growth can dry up rapidly in bear markets. Second and even more important, exit prices and the resulting returns to private equity investors are correlated with the global equity markets, decreasing the appeal of private equity as an investment instrument (Gaspar, 2007). Also, surveys have shown that the public generally knows very little about the methods and procedures of private equity and venture capital players. Therefore, if the capital base is to be improved, the industry will have to provide more information and improve its reputation by clearly informing the public of its true economic impact (Marchart, 2007).

1.1.4 Private Equity and Venture Capital Performance in Europe by Country

Despite these challenges, the overall performance of the European private equity and venture capital industry has never been better, and 2006 clearly was a record year. For the first time, European private equity fundraising reached €112 billion, an increase by 57% compared to the previous year, with investments in the range of €71 billion – or a 50% rise compared to 2005 – into more than 7500 companies (Marchart, 2007). Figure 1.2 shows the private equity and venture capital investment

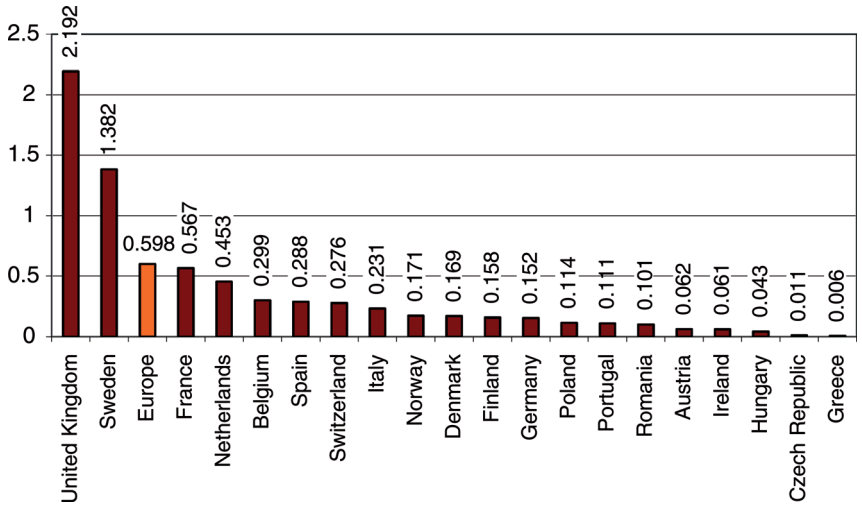

Figure 1.2 Private equity and venture capital investment in Europe, percentage share of the 2006 growth domestic product (European Venture Capital Association, 2007b).

proportion as a percentage of the 2006 growth domestic product (GDP) for the different European countries. Two countries were far ahead of the average, namely UK and Sweden.

1.1.5 The Future of Private Equity and Venture Capital in Europe

Many financial experts believe that a new era has just begun. Not only are today's investors fewer, smarter, more disciplined, and have a more global outlook, they also work with smarter entrepreneurs, many of whom are serial entrepreneurs. According to the German-based Center of Private Equity Research (CEPRES; www.centerofprivateequityresearch.de), better investment selection combined with a strong economic backdrop have led to the highest returns ever.

In addition, according to a recent survey done by the European Venture Capital Association (EVCA; www.evca.com), tax policies and legal codes appear to have become more favorable to private equity and venture capital in most European countries. These changes are reflected impressively in the Private Equity Performance Index (CepreX) provided by CEPRES. CepreX derives from the performance of several hundreds of individual transactions. The partial index for venture capital increased significantly in the past few years and in September 2006 reached a level of more than 26% higher than in the year 2000, the pinnacle of venture before its post-bubble nosedive (Figure 1.3; CEPRES; Romaine, 2007). The future of the European venture capital industry also looks bright, thanks to the mix of low capital volume in the market, a booming economy, and a steep learning curve for venture capital managers, and the European venture market place is expected to continue its rise (Herzog, 2007).

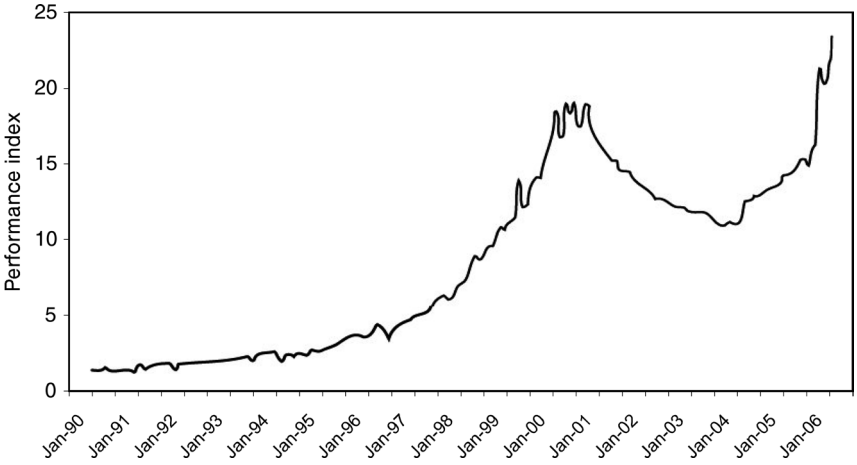

Figure 1.3 European venture performance index CepreX from 1990 to 2006 (CEPRES; Romaine, 2007). The figure shows the gross development of private equity transactions. Fund fees are not included. Therefore, the index development shows the annual return of real deals (company transactions) and not net to the limited partners.

1.2 Development of the Biotech Industry

1.2.1 Definition

By definition, 'biotech' companies are companies whose primary commercial activity relies on the application of biological organisms, systems, or processes or on the provision of specialist services to facilitate the understanding thereof (Hodgson, 2006). The term 'biotechnology' means any technological application that uses biological systems, living organisms, or derivatives thereof to make or modify products or processes for specific use. Biotechnology has applications in four major industrial areas, i.e., health care, crop production and agriculture, nonfood uses of crops and other products (e.g., biodegradable plastics, vegetable oil, biofuels), and environmental uses.

A series of derived terms have been coined to identify several branches of biotechnology, most importantly the white, or industrial biotechnology, focusing on the use of enzymes as industrial catalysts to either produce valuable chemicals or destroy hazardous chemicals, and red biotechnology as applied to medical processes, such as the design of organisms to produce antibiotics or the engineering of genetic cures through genomic manipulation (European Association of Bioindustries; www.europabio.org).

The development of new drug compounds is a complex, long, and costly process. Figure 1.4 describes the product development cycle for a typical new chemical entity

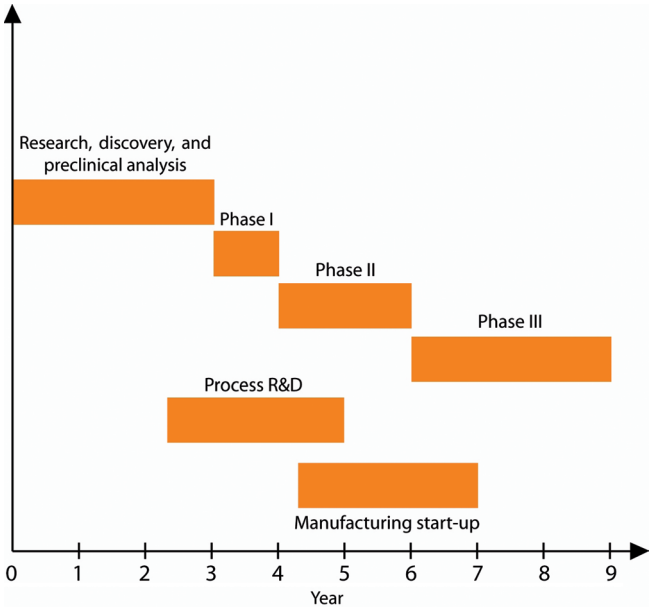

Figure 1.4 The product development cycle of a new chemical entity (Pisano, 1997).

(NCE), starting at the time the entity is discovered. The discovery process leading up to this point can take a number of years. For biotechnology products, or new biological entities, the drug development process is similar to that of NCEs – except that the process R&D and manufacturing start-up begin earlier – with the product development cycle of a new biotechnology-based drug starting when the genes for a specific protein molecule have been cloned (Pisano, 1997).

Once the chemical lead has been discovered or the biological developed, the preclinical research phase begins, with the target to obtain information about the molecule's safety and therapeutic properties. The main goals of preclinical studies are to determine a drug's pharmacodynamics, pharmacokinetics, and toxicity. This stage typically involves subjecting it to a series of screens or tests in both test tubes and laboratory animals. After the company has achieved reasonable confidence in a compound's safety and therapeutic benefits, the next major stage of drug development is human clinical trials. In Phase I clinical trials, the drug is administered to a small sample of healthy volunteers. These trials are designed to determine the drug's safety. Phase I clinical testing also seeks to find out how the pharmaceutical is absorbed and distributed, how long it is active in the body, how it is metabolized by the body, and how it is excreted. The conclusion of Phase I testing leads to Phase II testing, whose primary purpose is to determine whether the drug works, i.e., the drug's pharmaceutical efficacy. Phase II trials also determine the appropriate dosage regime (such as 2.5 mg twice per day, or 5.0 mg once per day) and the form of the drug (such as tablet, capsule, or liquid). In general, the end of Phase II trials marks an important project milestone (Pisano, 1997).

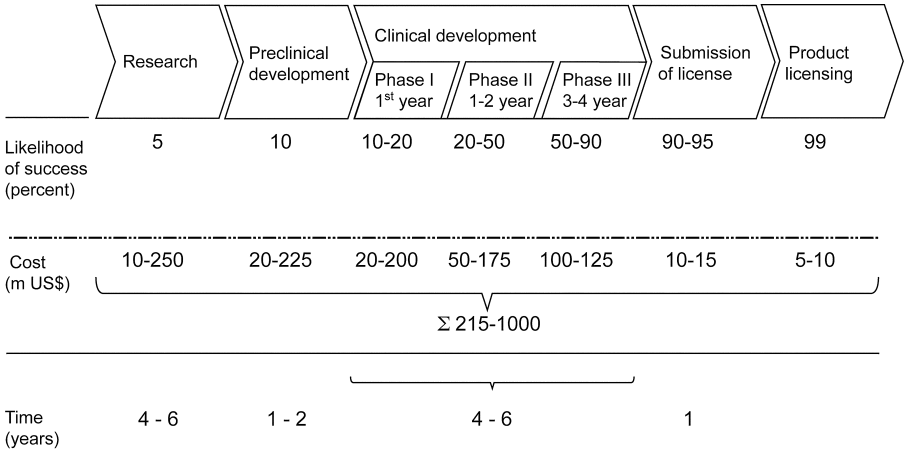

Figure 1.5 Biotech products take time, require significant investments, and carry considerable risk (US$ million; Dewasthaly, 2007).

Companies review the data obtained in Phase I and Phase II studies very carefully before they make a 'go or no-go' decision on Phase III. Phase III trials, which involve head-to-head comparisons of the new drug against placebo or existing drugs in a large sample of patients, are by far the most costly phase of human clinical trials. It is important to bear in mind that ultimate commercialization is by no means assured simply because a company reaches Phase III clinical trials: approximately 13% of new chemical entities are abandoned after the start of Phase III trials. After successful completion of Phase III trials, the company submits its clinical data for review to authorities like EMEA in Europe and FDA in the US (Pisano, 1997). The entire product development time from research to product licensing ranges over 10–15 years, with associated costs ranging from US$215 million to US$1 billion (Figure 1.5; Dewasthaly, 2007).

1.2.2 Historical Background

In the late 1950s, the biotech industry did not exist, because the key scientific breakthroughs ultimately responsible for its emergence had yet to occur. It still took more than two decades until the first biotech company, Genentech, was founded in the US. The basis for this foundation was the successful invention of a technique for manipulating the genetic structure of cells to synthesize specific proteins, developed in 1973 by Herbert Cohen and Stanley Boyer of the University of California. Genetic engineering first enabled the development of a wide range of proteins into therapeutic drugs. Within months of Cohen and Boyer's invention, Genentech was formed by Robert Swanson as young venture capitalist and Boyer as co-founder (Pisano, 1997).

In 1978, Genentech closed an agreement with the American pharmaceutical company Eli Lilly, granting Lilly the rights to manufacture and market recombinant insulin for diabetes treatment. In return, Lilly agreed to finance development of the product and to pay Genentech sales-dependent licensing fees. This agreement removed one of the biggest barriers for newly founded companies eager to step into the pharmaceutical business: the large amounts of money needed to finance the expensive R&D development time (Pisano, 2006).

The year 1980 witnessed the public listing of Genentech, and in 1982, the US Food and Drug Administration (FDA) approved insulin for marketing. Many other companies followed the successful example of Genentech, such as Amgen, Biogen Idec, Chiron (now Novartis), and Gilead Sciences (Pisano, 2006). Off to a slower start, the biotech industry in Europe started their attempt to catch up with US biotech developments in the 1990s, with companies such as Serono (now Merck Serono, Switzerland) and Union Chimique Belge (UCB, Belgium) among them. Scientific landmarks that accompanied these developments included the discovery of restriction enzymes, the first transfer of genetic material, and the development of early DNA sequencing methods in the early to mid-1970s, complemented by the invention of polymerase chain reaction (PCR) in 1983 and the completion of the genome sequences for organisms such as drosophila, mouse, and ultimately, humans (Küpper, 2006).

The progress of the industry is reflected by recombinant biological products meanwhile having established markets with multibillion dollar sales, such as erythropoietin, insulin, interferons, monoclonal antibodies, and human growth factors. To date, more than 155 biotech drugs and vaccines have been approved by the FDA and over 370 biotech products and vaccines are currently in clinical testing, targeting more than 200 diseases (Küpper, 2006).

The area of biotechnology has developed into a large, research-intensive industry with more than 4000 companies worldwide and parallel financing and venture capital funding to match. As the largest biopharmaceutical market in the world, the US has benefited greatly from the latest drugs and advances to emerge from biotechnology. In 2006, more than 300 public biotechnology companies in the US were employing over 130 000 people and represented about US$400 billion in market capitalization (Table 1.1; Ernst & Young, 2007).

Table 1.1 Global biotechnology at a glance in 2006 (Ernst & Young, 2007).

	Global	US	Europe	Canada	Asia-Pacific
Public company data					
Revenues (US$ million)	73 478	55 458	11 489	3242	3289
R&D expenses (US$ million)	27 782	22 865	3631	885	401
Net loss (US$ million)	5446	3466	1125	524	331
Number of employees	190 500	130 600	39 740	7190	12 970
Number of companies					
Public companies	710	336	156	82	136
Public and private companies	4275	1452	1621	465	737

Table 1.2 Pipeline of European biotech companies listed on stock exchanges by clinical development phase in 2006 (Ernst & Young, 2007).

Country	Preclinical	Phase I	Phase II	Phase III	Total
UK	99	31	79	37	246
Switzerland	39	14	21	23	97
Germany	37	17	16	7	77
Denmark	28	18	26	5	77
France	17	10	12	3	42
Sweden	14	11	6	5	36
Norway	6	5	5	1	17
Israel	5	3	6	2	16
Belgium	10	1	5	–	16
Ireland	5	3	6	1	15
Italy	6	1	5	2	14
Austria	9	3	1	1	14
Netherlands	4	6	2	1	13
Finland	4	–	1	2	7
Iceland	–	1	4	–	5
Total	283	124	195	90	692

In Europe, the general slowdown in the global economy between 2001 and 2004 also reflected negatively on the European biotech industry. Back on track in 2005, the year 2006 can be qualified as a year where Europe regained its momentum and displayed newly found strengths on every front.

First, the European biotech industry succeeded in growing their pipelines and leading a considerable amount of new chemical and biological entities into the next development phase. Tables 1.2 and 1.3 provide an overview of the pipelines of listed and unlisted European biotech companies by clinical development phase in 2006.

Second, the European biotech industry managed to attract new investors and to show solid growth of key financial metrics, such as a revenue growth of 13% between 2005 and 2006 (Table 1.4). Research and development (R&D) expenses continued to increase and kept pace with rapidly growing revenues as companies realized that R&D investments remain critical to generating value in the long run (Ernst & Young, 2007).

1.2.3 Financing Biotech Start-ups

Each development phase of a start-up company is financed by specific types of investors. In the preseed or seed phases, financing is usually accomplished by sources including the 'three Fs,' i.e., 'family, friends, and fools', as well as government and EU funds. Further on, business angels, and more frequently early-stage venture capitalists continue investing in the start-up. In later development stages, strategic

Table 1.3 Pipeline of European biotech companies not listed on stock exchanges by clinical development phase in 2006 (Ernst & Young, 2007).

Country	Preclinical	Phase I	Phase II	Phase III	Total
Germany	69	21	52	9	151
UK	40	33	30	3	106
France	51	13	19	2	85
Denmark	36	20	16	2	74
Switzerland	30	14	18	7	69
Israel	33	14	18	2	67
Sweden	29	4	14	2	49
Italy	28	10	8	1	47
Austria	30	5	6	4	45
Spain	19	6	7	5	37
Netherlands	15	2	6	1	24
Belgium	13	3	3	5	24
Norway	4	–	9	–	13
Ireland	6	–	5	–	11
Total	403	145	211	43	802

alliances with corporate companies become essential, as are deals with late-stage venture capitalists.

Important liquidity events for already matured companies are initial public offerings (IPOs) and secondary public offerings. An IPO is the first sale of stock by a private company to the public. One important reason for why a private company may wish to go public is to raise capital. A secondary public offering, usually done within a few years following an IPO, is an excellent method for a company to raise additional working capital. There are two main types of secondary public offerings. Thus, an issuer offering involves the issuance of new stock, diluting the ownership position of stockholders who own shares that were issued in the IPO. Alternatively,

Table 1.4 European biotechnology in 2006 and 2005 (Ernst & Young, 2007).

	Public companies			Industry total		
	2006	2005	Change	2006	2005	Change
Financial values (€ million)						
Revenues	9150	7993	14%	13 307	11 765	13%
R&D expenses	2892	2559	13%	5695	5259	8%
Net loss	876	1395	–37%	2541	3280	–23%
Market capitalization	62 165	43 374	43%	–	–	–
Industrial data						
Number of companies	156	122	28%	1621	1613	0%
Employees	39 740	34 250	16%	75 810	68 440	11%

Table 1.5 Financing of biotech companies: US vs Europe in 2005 and 2006 (US$ million; Ernst & Young, 2007).

	2006		2005		Change	
Type	**US**	**Europe**	**US**	**Europe**	**US**	**Europe**
IPO	944	907	626	691	51%	31%
Follow-on and other offerings	16 067	3069	10 740	1577	50%	95%
Venture financing	3302	1907	3328	1738	−1%	10%
Total	20 313	5883	14 694	4006	38%	47%

one or more major stockholders in a company may sell all or a large portion of their holdings. Because no new shares are released, the owners' holdings are not diluted.

In 2006, investors committed a total of more than US$26 billion in the biotech industry, an upswing of 42% compared to previous year (Table 1.5). Venture capital for the first time reached an alltime high of US$5.2 billion. Overall, capital raised increased by 38% in the US and by 47% in Europe (Ernst & Young, 2007).

In Europe, all of these elements, i.e., IPOs, follow-on offerings, and venture financing, contributed to a very strong year 2006, with a grand total of US$5.9 billion, or approximately €4.7 billion, for the entire industry (Table 1.5). By comparison, the increase between 2004 and 2005 was a mere 18%. A total of 32 companies went public in 2006. While the importance of IPOs and follow-on financing vehicles increased, venture capital investments did not hold path to the same degree. Even so, the overall amount of venture capital raised by European biotech companies in 2006 set an alltime record, passing US$1.9 billion, or approximately €1.5 billion, for the first time ever (Table 1.5, Figure 1.6; Ernst & Young, 2007).

Overall, venture capital expenditures differed greatly between countries. While France and some smaller countries, such as Belgium, Spain, and Austria,

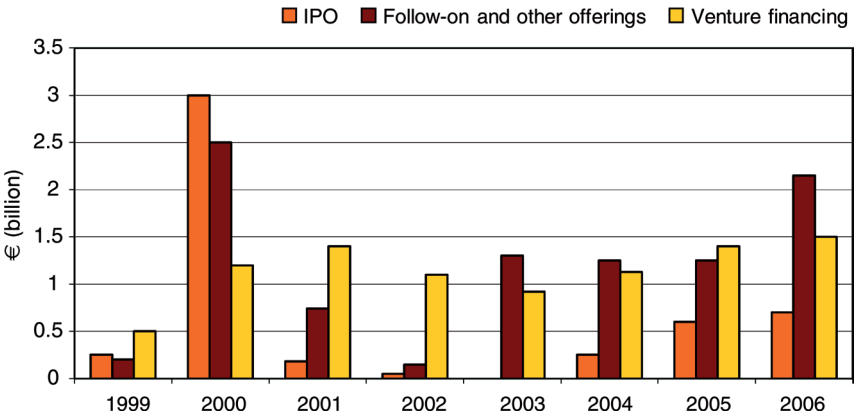

Figure 1.6 Summary of European biotech financing (€ billion), 1999–2006 (Ernst & Young, 2007).

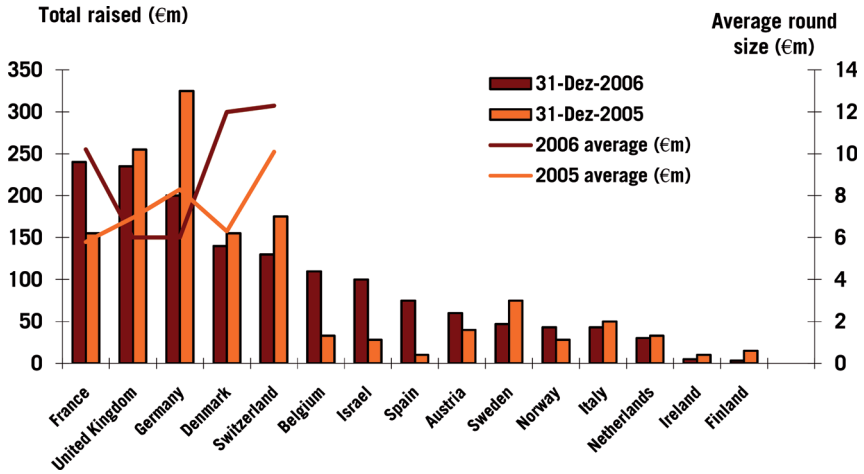

Figure 1.7 European venture capital by country (€ million), 2006 and 2005 (Ernst & Young, 2007).

significantly increased their venture capital volume, others, including Germany and Switzerland, experienced declines relative to 2005. In Germany, the reason was the preponderance of early-stage deals with lower average round sizes, while in Switzerland, the decline resulted from 2005 having been an exceptionally strong year, in part because of two pre-IPO rounds raised by Speedel, totaling €76 million (Figure 1.7; Ernst & Young, 2007).

With regard to IPOs, the industry's market capitalization took a big step forward in 2006 (Figure 1.8), with a 43% upswing compared to the previous year (Table 1.4; Ernst & Young, 2007). Public investors who in previous years had invested elsewhere, began to regain trust in biotech and even supported public offerings of relatively young companies.

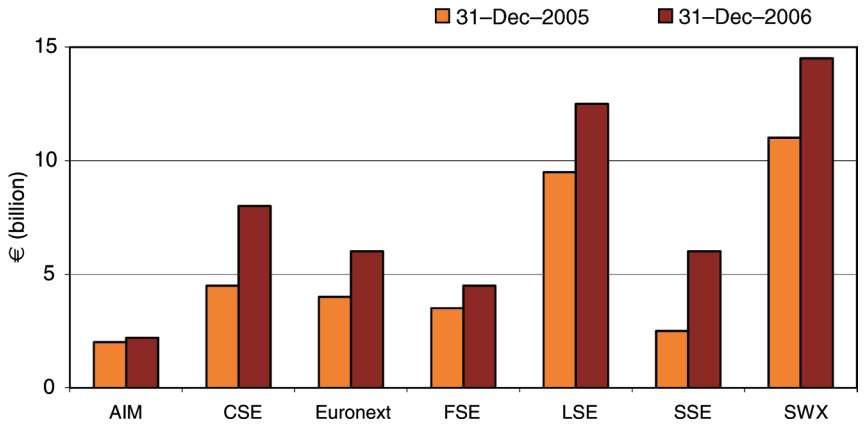

Figure 1.8 Market capitalization of biotech companies by main European stock markets (€ billion; Ernst & Young, 2007).

Total market capitalization of the IPO class was €3.5 billion in 2006, almost identical to 2005. Fundraising success varied from exchange to exchange. The Swiss exchange (SWX) in Zurich proved outstanding both in terms of capital raised and average deal size. Surprisingly, the London Stock Exchange (LSE) and the Frankfurt Stock Exchange (FSE) were less successful. With a total of eight IPOs and €107 million raised, the Alternative Investment Market (AIM) in London attracted the highest number of deals and achieved a similar ranking as the stock market in Copenhagen (CSE) and Euronext. AIM was generally used by smaller enterprises with lower capital needs (Figure 1.8; Ernst & Young, 2007).

1.2.4 Exit Routes in the Biotech Industry

From the beginning, investors are generally motivated by a clear idea of the exit strategy of a young company and the method through which they can cash in on their investment. During their long development times, most biotech start-ups try to set up parallel exit options, ultimately enabling them, together with their investors, to pick the best strategy to realize the inherent value of the company. In the biotech industry, the most frequent exits are trade sales and IPOs.

For an IPO to be successful, the company first has to invest enormous amounts of time and money into building a pipeline that is likely to attract investors. For many European biotech companies, the price of establishing such a pipeline is too high relative to what can be raised on the public markets. Moreover, having gone public, young biotech start-ups will be challenged by a much higher visibility and receive increased scrutiny from both the media and financial analysts, particularly if the first products have not yet reached the market.

Therefore, investors and companies are looking at trade sales as an alternative route (Ernst & Young, 2007). Acquisition activity has recently heated up, and the reasons for this are manifold. The lackluster IPO market, the high price of licensing deals that have made outright acquisitions more attractive, an opportunity for pharmaceutical companies to repatriate foreign earnings, new requirements on public companies in the form of Sarbanes–Oxley, and new restrictions on analysts all work together to fuel this trend (Levine, 2005).

Finally, another exit strategy is the MBO, i.e., managers or executives of a company purchase the controlling interest in a company from existing shareholders. This is usually not a viable option for biotech companies, because their entrepreneurs do not dispose over such high capital needs.

In the first six months of 2007, an amazing 37 biotech firms went public worldwide, compared to 50 IPOs in the whole of 2006. Most of the newly listed companies were based in North America and Europe. North America had 15 companies involved in IPOs and Europe had 14, overshadowing China with four, Israel with three, and Australia with one (Scrip, 2007b).

Moreover, in 2006, the European biotech industry continued to engage in mergers, acquisitions, and alliances. While the number of M&A transactions was flat, many individual transactions were interesting with regard to valuations and targets. In a

global trend, pharmaceutical companies around the world invested large amounts of money in biotech companies with promising platforms in areas such as antibodies or vaccines, as they sought to buy what they hoped could become the engines for new generations of cutting-edge products. On the alliance side, there has been a recent shift to early-stage deals with companies covering broad applications through innovative platforms or individual products with treatment options in several indications (Ernst & Young, 2007).

1.2.5
The Challenges to European Biotech

Today, the European biotech industry accounts for close to 75 000 jobs and over 1600 companies. While the expansion of the EU has brought significant new opportunities to the European biotech industry, including cost advantages, it has also increased the legal and regulatory complexity of developing a drug candidate through to approval by the European Medicines Agency (EMEA; Ernst & Young, 2007).

Moreover, as indicated earlier, it has become tougher for companies to raise venture capital. The reasons for this are manifold. For one thing, consolidation has thinned the ranks of venture capital firms. Also, the vibrant European IPO market, swallowing large amounts of capital, may have reflected negatively on the venture capital environment. The increasing complexity of venture capital consortia, dilution and liquidation preference issues, and valuation discrepancies have further aggravated the situation. Another challenge has to do with the increasing unwillingness of venture capitalists to fund discovery or early stages of clinical development. The companies suffering most from this funding gap are in critical development phases, where product candidates have emerged but financial support for proof-of-concept clinical studies is lacking. At the same time, proof-of-concept is the most important decision factor for successful investment decisions.

While aggregate fundraising was high, the number of rounds fell and average capital raised per round increased. More money seems to have been made available, but it went to fewer companies. With the venture capital focus on late-stage companies (Figure 1.9), the question is how young biotech start-ups will attract the capital needed, and this will increase the overall challenge on the industry's sustainability (Ernst & Young, 2007).

1.2.6
The Future of the European Biotech Industry

Next to private equity and venture capital fund raising, additional opportunities for entrepreneurs seem to be developing, especially through newly installed EU public policy pathways. In March 2000, the Lisbon Agenda was adopted, with the goal to make Europe the "most competitive and the most dynamic knowledge-based economy in the world by 2010" (European Commission; http://ec.europa.eu/growthandjobs/index_en.htm). To achieve the Lisbon objectives and to encourage R&D, the EU initiated the Seventh Framework Program for Research and Technical

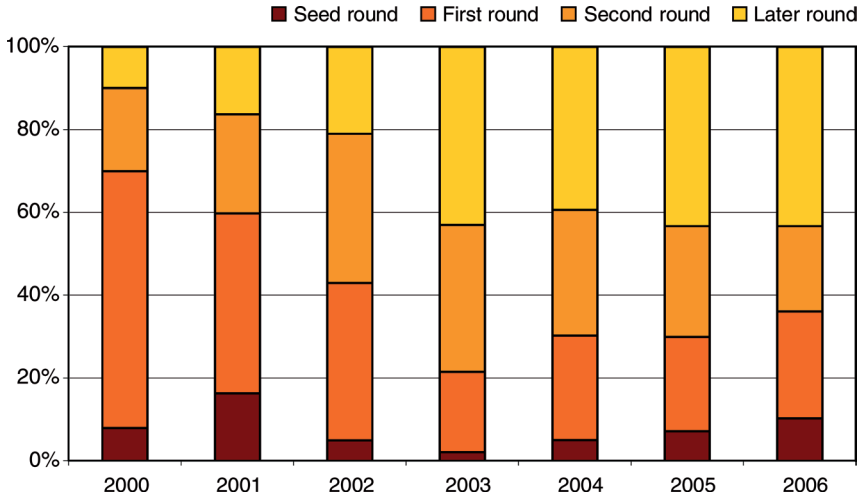

Figure 1.9 European venture funding by round class, 2000–2006 (Ernst & Young, 2007).

Development (FP7) in funding food, agriculture, and biotechnology research, with an overall budget of €53.2 billion from 2007 through 2013 (Figure 1.10; Community Research & Development Information Service; http://cordis.europa.eu). This budget was divided up among the following areas by an indicative breakdown:

- Collaborative research ('cooperation'), supporting all types of research activities carried out by research bodies in transnational cooperation targeted to gain or consolidate leadership in key scientific and technology areas

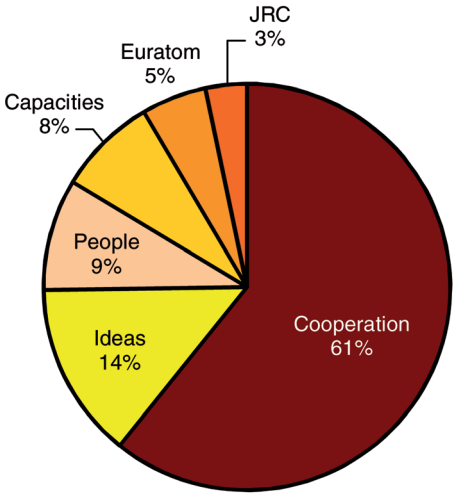

Figure 1.10 Indicative breakdown of the FP7 (http://cordis.europa.eu).

- Frontier research ('ideas') within the framework of activities commonly understood as 'basic research,' targeted to produce new knowledge leading to future applications and markets
- Marie Curie Actions ('people'), a program dedicated to stimulating researchers' career development, mobility, and training
- Research capacity ('capacities'), a program complementary to the cooperation program aiming to enhance research and innovation capacities throughout Europe as well as their optimal use (e.g., support for the coherent development of policies)
- EURATOM, carrying out energy research activities for nuclear research as well as training activities
- Joint Research Centre (JRC), providing customer-driven scientific and technical support to the conception, development, implementation, and monitoring of EU policies. Priorities include competitiveness and innovation, supporting the European Research Area (ERA), research in the areas of renewable and cleaner energies and transport, life sciences, and biotechnology.

The collaborative research program, called 'cooperation,' with an overall budget of €32.4 billion, is supposed to bring together the best talents from across Europe to tackle areas such as health, food, agriculture, biotechnology, energy, and the environment. Figure 1.11 provides a detailed overview of spending per area.

Since their launch in 1984, the Framework Programs have played a lead role in multi-disciplinary research and cooperative activities in Europe and beyond. FP7

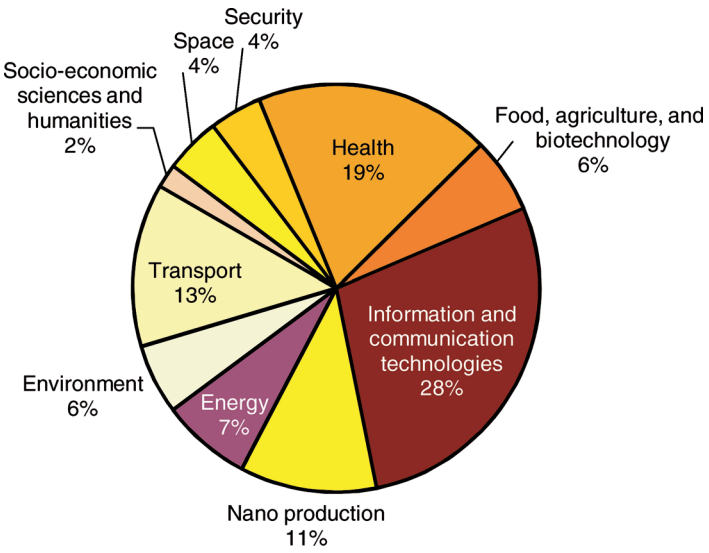

Figure 1.11 Distribution of funds spent on the collaborative research program (http://cordis.europa.eu).

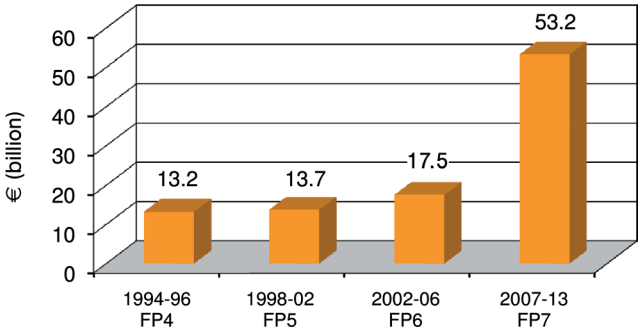

Figure 1.12 Evolution of EU research framework program budgets (€ billion; http://cordis.europa.eu).

continues this task and is also both larger and more comprehensive than earlier Framework Programs. FP7 reflects the largest funding allocation yet, representing an enormous increase in budget compared to FP6 (Figure 1.12).

Participation in FP7 is open to a wide range of organizations and individuals, including universities, research centers, multinational corporations, small to medium-sized enterprises, public administrations, and even individuals.

Beyond FP7, there seem to be continuous and increasing efforts within the EU to set up better frameworks and incentives that use state aid as an instrument to boost research, development, and innovation. One case in point is the new Research, Development and Innovation (R&D&I) Framework, which took effect on 1 January 2007 and set out a series of guidelines for specific types of state aid measure – such as aid for R&D projects, aid to young innovative enterprises, and aid to innovation clusters – that could encourage additional R&D&I investments by private firms, thus stimulating growth and employment and improving Europe's competitiveness (Ernst & Young, 2007).

Overall, the most encouraging news in Europe in 2006 was related to the field of product development, and this is expected to continue in 2007 and beyond. With wider and more mature pipelines, European companies should be well poised to bring innovative new products to the market. Ultimately, the ability to deliver on that promise will become the true determinant of sustainability (Ernst & Young, 2007).