Do Financial Markets Support Innovation or Inequity in the Biotech Drug Development Process?

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1. The publicly listed company in biopharmaceuticals

Biotech drug development is a very costly and highly uncertain process. One has to expect the passage of at least ten years from the time a company launches the development of a particular drug to the time it generates a commercial product. If the total cost of developing the drug were to be, say, €500 million, it would be seen as a relatively inexpensive investment for this industry. Even then, no one can claim with any degree of certainty that even after years of drug development a commercial product will emerge.

Yet, notwithstanding the cost and uncertainty of the drug development process, as can be seen in Table 1, there are thousands of biotech companies in existence, with the vast majority of them being privately held.[1] The publicly-listed company is in particular an American phenomenon; in 2009 the United States had 50 percent of public companies. Although Europe had more biotech companies, public and private combined, than the United States (1,790 versus 1,699), its 171 public companies were 55 percent of the US number. Moreover, on a per company basis European public companies were much smaller than US public companies, with only 54 percent of the revenues, 50 percent of the R&D expenditures, and 82 percent of the employees.

Table 1. Publicly-listed biotechnology companies, by geographic region, 2009

	Global	USA	Europe	Canada
Public company data				
Revenue, US$b	79.1	56.6	16.6	2.2
R&D expense, US$b	22.6	17.2	4.7	0.4
Net income (loss), US$b	3.7	3.7	(0.4)	(0.1)
Number of employees	176,210	109,100	49,120	6,930
Number of companies				
Public companies	622	313	171	64
Private companies	na	1,386	1,619	260

Source: Ernst & Young, *Beyond Borders: Global Biotechnology Report, 2009*

The United States has a longer history of public biotech companies – going back to the celebrated initial public offering (IPO) of Genentech in 1980 – in part accounting for their larger average size when compared with Europe. In addition, as shown in Table 2a, the number of public companies in Europe increased rapidly from 2003 to 2007, with, as indicated in Table 2b, the average size per company falling as new, generally smaller, companies did their IPOs. Notwithstanding the small profit (6.5 percent of sales) turned by US public companies in 2009, the historical experience of the both the US and European biotech industries has been one of persistent losses. Nevertheless, from 2008 to 2009, the data reveal an overall increase of 8 percent in the revenues of European companies compared with a 13 percent decline for US companies.

[1] Note that the Ernst & Young data include all independent biotechnology companies, not just biopharmaceutical companies. Moreover, these revenues do not include the biopharmaceutical revenues of "big pharma" companies, which, as Lazonick and Tulum (2009) have shown, are substantial.

Table 2a. Public biotech companies in USA and Europe, revenues, R&D expenses, net income, and employees, 2001-2009

Data for public companies, except "All companies

	2001	2002	2003	2004	2005	2006	2007	2008	2009
USA									
Revenue, US$b.	24.4	30.3	35.9	42.7	47.8	55.5	84.9	65.1	56.6
R&D expense, US$b	11.4	16.3	13.6	15.7	16.0	22.9	31.8	22.6	17.2
Net income, US$b	-4.8	-9.7	-3.2	-4.3	-2.1	-3.5	-2.7	0.4	3.7
Employees (000s)	126.0	142.9	146.1	137.4	na	130.6	134.6	120.3	109.1
Public companies	342	318	314	330	329	336	386	366	313
All companies	1,457	1,466	1,473	1,444	1,415	1,452	1,502	1,771	1,699
EUROPE									
Revenue, US$b	7.5	8.3	7.5	7.7	9.8	11.5	12.9	15.4	16.6
R&D expense, US$b	4.2	5.0	4.2	4.2	3.3	3.6	4.6	4.8	4.7
Net income, US$b	-0.6	-2.8	-0.5	-4.8	-1.9	-1.1	-1.7	-1.3	-0.4
Employees	34.1	33.3	32.5	25.6	na	39.7	47.7	48.4	49.1
Public companies	104	102	96	98	122	156	181	179	171
All companies	1,879	1,878	1,861	1,815	1,613	1,621	1,744	1,819	1,790

Source: Ernst & Young, *Beyond Borders: Global Biotechnology Report, 2002-2009*

Table 2b. Public biotech companies in USA and Europe, average per company revenues, R&D expenses, net income, and employees, 2001-2009

	2001	2002	2003	2004	2005	2006	2007	2008	2009
USA									
Revenue, US$m	71.3	95.2	114.2	129.5	145.3	165.1	219.6	177.9	180.8
R&D expense, US$m	33.4	51.2	43.2	47.6	48.6	68.1	82.4	61.8	55.0
Net income, US$m	-14.2	-30.6	-10.3	-13.1	-6.5	-10.3	-7.0	1.1	11.8
Employees	368	449	465	416	na	389	349	329	349
EUROPE									
Revenue, US$m	72.4	81.0	77.8	78.9	80.2	73.6	71.5	85.8	97.1
R&D expense, US$m	40.8	48.9	44.1	42.4	26.8	23.3	25.2	26.9	27.5
Net income, US$m	-5.8	-27.1	-5.7	-4.9	-15.9	-7.2	-9.3	-7.1	-2.4
Employees	329	327	338	262	na	255	264	271	287

Source: Ernst & Young, *Beyond Borders: Global Biotechnology Report, 2002-2009*

Despite the lack of profitability, substantial investment capital has flowed into the global biotech industry through venture capital, initial public offerings, and follow-on offerings, typically in the form of secondary public offerings but at times convertible debt issues. As shown in Table 3, the United States has generally had much higher levels of venture capital investment in the biotech industry than Europe; for 2001-2008 $32 billion for the United States compared with $15.3 billion for Europe. So too with funds raised through IPOs, with an eight-year total of $6.2 billion for the United States and $3.4 billion for Europe. It is however in follow-on financing that totaled $97.2 billion over this period that the United States far outstrips Europe, which raised only 18 percent of that amount.

Table 3. Sources of investment capital for US and European biotech companies, 2001-2009

	2001	2002	2003	2004	2005	2006	2007	2008	2009
USA									
Venture capital, US$b	2.4	2.2	2.8	3.6	3.3	3.3	5.5	4.4	4.6
Initial public offering, US$b	0.2	0.5	4.4	1.6	0.6	0.9	1.2	0.0	0.7
Follow-on and other, US$b	5.3	6.1	11.1	11.8	10.7	16.1	14.7	8.5	12.8
EUROPE									
Venture capital, US$b	1.4	1.2	3.6	1.4	1.7	1.9	1.6	1.4	1.1
Initial public offering, US$b	0.2	0.0	0.0	0.4	0.7	0.9	1.0	0.1	0.1
Follow-on and other, US$b	0.7	0.1	0.21	1.6	1.58	3.1	4.9	1.1	2.8
Ratio EUROPE:USA									
Venture capital	0.57	0.53	1.26	0.41	0.52	0.58	0.29	0.31	0,24
Initial public offering	0.84	0.06	0.00	0.22	1.10	0.96	0.82	18.50	0,21
Follow-on and other	0.14	0.02	0.14	0.14	0.15	0.19	0.33	0.13	0,22

Source: Ernst & Young, *Beyond Borders: Global Biotechnology Report, 2002-2009*

With the financial crisis of 2008, the market for biotech IPOs virtually dried up. In its lead article, "Beyond business as usual?" in its 2009 *Beyond Borders* review of the global biotech industry, Ernst & Young (2009, 3) observed:

> In the past, biotech funding droughts have largely been driven by investor sentiment toward the biotech industry. When investors were bullish about the sector's prospects – buoyed, for instance, by product approvals in the industry's formative years or by media excitement of over the sequencing of the human genome around the turn of the millennium – money rushed into the sector, and companies rushed out to conduct IPOs. Unfortunately, the boom was inevitably followed by a bust a few years later, when investors realized that the path to commercialization was considerably longer than they had initially assumed or when business models failed to live up to their promises. Funds withdrew, bubbles burst, windows slammed shut.
>
> The current funding crisis is different. The bubble that burst was not in biotech, but fuelled by real estate, financial instruments and an environment of easy credit. This time, irrationally exuberant investors were seduced by loose lending practices, high-leverage models and the assurances of complex financial derivatives that promised to hedge and reduce risk. And so, while biotech's past financing droughts were localized and industry-specific, the present downturn crosses national boundaries and impacts industries across the economy. It is, in a word, *systemic*.

Nevertheless, even in the crisis years of 2008-2009, $31 billion in private and public equity flowed into the US biotech industry. Of $127 billion in revenues for public biotech companies, $21 billion were non-product revenues, much of which came from R&D contracts with large established pharmaceutical companies. In 2008 and 2009 public companies in the US biotech industry spent over $42 billion on R&D (Ernst and Young 2009, 34 and 2010, 59).

In his 2006 book, *Science Business: The Promise, the Reality, and the Future of Biotech*, Gary Pisano emphasized the unprofitability of the US biotechnology industry throughout its history, but nevertheless recognized that the industry had received substantial amounts of business funding in the forms of private equity, R&D contracts, and public equity. William

Lazonick and Oner Tulum (2009) have dubbed this apparent contradiction "the Pisano puzzle": Why has so much money, much of it in the possession of smart investors, flowed into an industry with such a long history of unprofitability? In their paper on US biopharmaceutical finance, Lazonick and Tulum (2009) offer a solution to the "Pisano puzzle" in terms of a combination of government funding and the speculative stock market.

Through the National Institutes of Health (NIH), the US government has spent in excess of $30 billion per year on life sciences research in the late 2000s, a budget that is twice in real terms what it was in the mid-1990s when the level of NIH funding was already very substantial. Indeed, since the first National Institute of Health was founded in 1938, the US government has poured over $706 billion in 2009 dollars into the life sciences knowledge base. Especially since the passage of the Bayh-Dole Act in 1980, commercial enterprises have been able to tap this government-funded knowledge base as well as government subsidies such as those under the Orphan Drug Act of 1983 (Lazonick and Tulum 2009).

Given the government-funded knowledge base and government subsidies, the prospect of a relatively quick "exit" through an IPO, or alternatively an M&A deal, has induced venture capitalists and big pharma to take private equity stakes in start-ups. Indeed, given the long gestation periods for drug development, some of these "start-ups" may have been in existence for a decade or more without a commercial product. The fact is, moreover, that virtually all biopharmaceutical IPOs in the United States are for companies that have yet to generate an approved drug. Stock-market investments in these productive-less IPOs are inherently speculative, with the buyer of the stock looking to reap a capital on "good news" and avoid a capital loss on "bad news". Indeed, as we shall show, in some cases product-less companies may stay in business for a decade or more even after their IPOs, and go to the stock market for follow-on offerings.

To some extent this combination of government funding and stock-market speculation also exists in Europe despite its low level of health-related governmental R&D expenditures. Larger European pharmaceutical companies such as Roche and Novartis have developed their own R&D capabilities in the United States to tap into the NIH-knowledge base. In 2001 the EU passed its own Orphan Drug Act. Europe, however, lacks speculative stock markets equivalent to NASDAQ; during the Internet boom of the late 1990s various European nations – for example the Nouveau Marché in France and the Neuer Markt in Germany – put such markets in place, but they collapsed in the early 2000s (Giudici and Roosenboom 2004; O'Sullivan 2007; Audretsch and Lehmann 2008).

A comparison of business models in European and US biopharmaceuticals offers, therefore, the possibility to assess the extent to which the combination of government-funded expenditures and speculative stock markets support or undermine the drug development process. The theoretical framework for this analysis is Lazonick's theory of innovative enterprise with its focus on strategic control, financial commitment, and organizational integration as social conditions for generating innovation, i.e., higher quality, lower cost products at prevailing factor prices (see Lazonick 2010 for a recent exposition of the theory, with references to empirical applications).

In particular, in project to which this paper is a contribution, we ask the following questions concerning the financing of European and US biopharmaceutical firms:

- How important have the government-funded knowledge base and government subsidies been in financing the drug development process?

- To what extent has the equity finance that has flowed into the biotech industry actually funded drug development?
- If this equity finance did not fund innovation, then how was it used and where did it go? Put differently, what is the relation between value creation and value extraction in a biopharmaceutical firm?

In the next section of the paper, we present a methodology based on case-study research for addressing these questions. In the following section we summarize evidence from four case studies, two of companies in the United States and two in Europe.[2] The material that we present shows the feasibility of doing the types of case study research that can provide a foundation for asking the innovation/inequity questions. In the final section of the paper, we draw some preliminary observations concerning the types of answers that one can derive from our case-study approach.

2. The need for a case-study approach

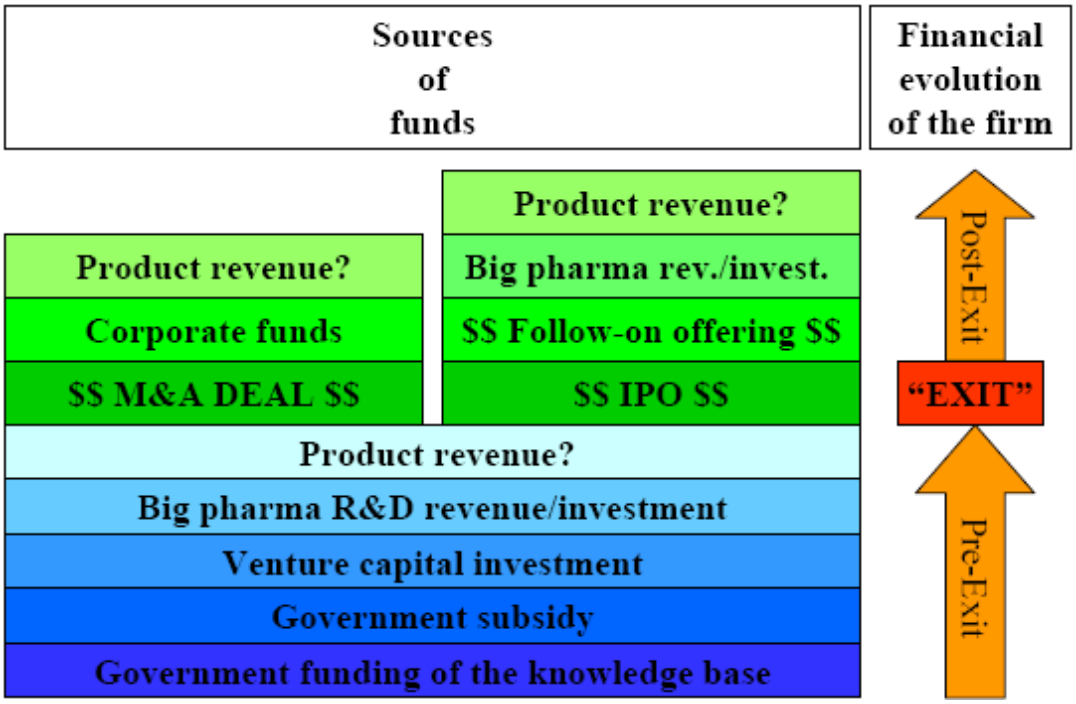
Our objectives in this research project are to understand the financial evolution of the firm – that is, its sources and uses of funds – and the impacts of this financial evolution on value creation and value extraction. Ideally, to carry out this analysis, we would possess a database on the sources and uses of funds as well the measures of value creation and value extraction that covers the relevant populations of firms (e.g., biopharmaceutical firms in Europe and the United States). The database could then be used to test alternative hypotheses of the impacts of financial institutions on innovation and/or inequity.

While there are a number of existing databases from which we can draw information on a number of variables, the existence of an integrated database with which to test alternative hypotheses concerning innovation/inequity remains to be constructed. As a critical step toward that goal, we have undertaken detailed case studies of the financial evolution of biopharmaceutical firms in order to develop a model of the phenomenon that captures the essence of the real-world experience of biopharmaceutical companies. These case studies may be useful in their own right – for example, our case study of Myriad Genetics which is at the center of landmark litigation concerning the right to patent a gene – but the larger purpose in doing them is to understand the dynamics of value creation/extraction for the sake of building databases for industry studies and policy analyses.

Figure 1 shows the types of firm-level data concerning the sources of funds that are relevant to this task (see Lazonick and Tulum 2009). In the biopharmaceutical industry, the foundation of finance of product development is government spending on the life sciences knowledge base – currently $30 billion per annum of NIH spending in the United States. Biopharmaceutical firms tap into this spending indirectly when, for example, they hire scientists but also directly when scientists associated with the company get NIH grants that are specific to its drug development process.

[2] The completed case studies are available from the authors.

Figure 1. The financial evolution of the firm in terms of the sources of funds

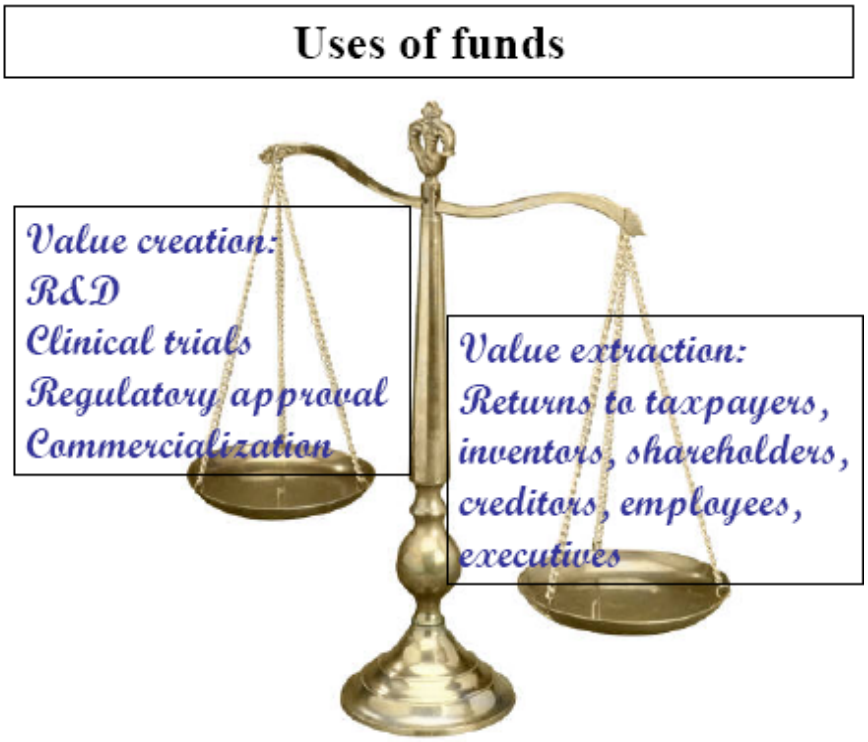


Source: Adapted from Lazonick and Tulum 2009.

Government subsidies to firms, such as those under the Orphan Drug Act can build on the government-funded knowledge base. It is at that point that opportunities for startups may be created for private equity, coming, for example, from venture capital and established corporations. Given the extraordinarily long time-frame and high-fixed costs of developing biopharmaceutical drugs, this private equity is lured into the industry by the prospect of a future "exit" from their investments either through an M&A deal with an established company or an IPO. These exits, which may occur with or without a commercial product, not only permit private equity holders to cash in on their investments but also can provide new sources of funds for the firm, either through internal investment subsequent to an M&A deal or public equity funds in the case of an IPO. For an independent biopharmaceutical firm, the stage is then set for follow-on public equity issues and R&D alliances with big pharma that typically entail a combination of revenues for contract R&D and public equity capital infusions.

Figure 2 provides a picture of the types of financial flows that enter into value creation and value extraction. It may well be, as depicted in Figure 2, that at any point in time value extraction has a greater weight than value creation, in which case, it will be necessary to fill the gap with sources of funds if the firm is to remain financially viable.

Figure 2. The financial evolution of the firm in terms of the uses of funds



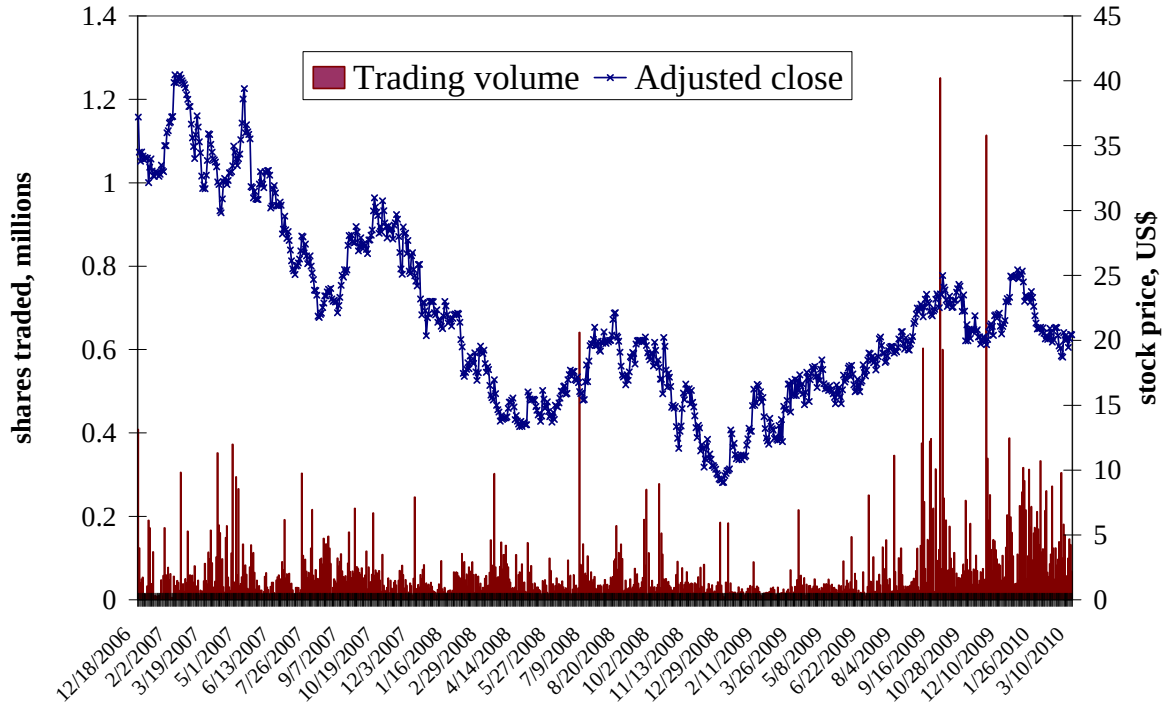
As an example of the relation between venture financing, R&D contracts, and IPOs in the financial evolution of a biopharmaceutical firm is Affymax. Founded in 1988 in The Netherlands with a research lab in Palo Alto, California, GlaxoSmithKline (GSK) acquired Affymax in 1995. Then in 2001 GSK spun off Affymax as an independent venture-backed private company. On December 15, 2006, Affymax did an IPO, raising $92 million.[3] From its founding to its IPO, Affymax recorded a total of $11.7 million in revenues, virtually all of it from an R&D partnership worth up to $102 million, inked in February 2006, with Japan-based Takeda Pharmaceutical. At that time, Affymax had a therapeutic product under development in the late stages of Phase II clinical trials, with the expectation of moving into Phase III trials in early 2007 and the possibility of gaining Food and Drug Administration (FDA) marketing approval for the drug in 2010; that is, three to four years after the IPO. At that point, Takeda would have exclusive rights to market the drug outside of the United States. But Takeda, as well as Affymax's venture capitalists, do not have to wait until a product actually goes to market to generate returns from their investments. As part of the R&D partnership, Takeda purchased 2.1 million Affymax shares for $10 million in February 2006. At the IPO some ten months later, Takeda's shares were worth $63 million.

Takeda was able to reap this return on its shareholdings because of the existence of public investors who were willing to speculate in the shares of a company like Affymax which was still years away from a commercial product. Indeed, from an IPO price of $30.00 on December 15, 2006, Affymax's stock rose to a peak price of $41.00 on February 12, 2007, and then began a general decline to a low (at the time of writing) of $9.03 on December 23, 2008. As can be seen in Figure 3, both the Affymax stock price and the trading volume in its

[3] Affymax had actually been founded in 1988 in The Netherlands with a research lab in Palo Alto, California. GlaxoSmithKline acquired Affymax in 1995.

shares have been very volatile, with speculators going into and out of the market in attempts to lock in speculative gains. The existence of stock-market investors looking to make speculative gains on a stock such as Affymax is what enables the IPO, which in turn attracts venture capital and big pharma money into the BP industry.

Figure 3. Stock-price movements and trading volume of Affymax shares, December 16, 2006-March 10, 2010



Note: Excludes trading volume of 1,997,500 shares on the IPO date, December 15, 2006.
Source: Yahoo! Finance

Given the roles of both government spending and the speculative stock market in financing biotech firms, there is a question of the extent to which financiers and speculators make money out of the biotech industry even when, as in the case of Affymax, a commercial product has yet to be generated and, indeed, there is no guarantee that a product ever will be generated. At the same time, there is a question of how and to what extent taxpayers, who collectively finance government spending, appropriate a return on their investments in the biotech industry. In cross-national comparative perspective, there is a question of whether in the long run the less highly financialized European business model in biotech is resulting, or will result, in superior drug development and a more equitable sharing of both the costs and benefits of the process.

To answer these questions, we have taken a case-study approach to the analysis of the biotech drug development process, using the theory of innovative enterprise as the analytical framework (Lazonick 2010). In seeking to determine the impact of strategic control on the drug development process, we analyze how those executives who make strategic decisions use their positions to allocate corporate resources. We document their educational backgrounds and their career trajectories. For public companies, we can also document their remuneration, including the extent to which they gain from stock-based pay, and especially

stock options. In seeking to determine the impact of financial commitment on drug development, we document the sources and uses of funds over the company's history. In particular, we ask whether through stock-based transactions some participants in the enterprise are positioned to extract more value than they help to create. In seeking to determine the impact of organizational integration on drug development, we document the evolution of employment at the company, including the types of personnel that the company has employed and the ways in which the company has attracted, retained, and motivated these people. Ultimately, with access to a particular company, we could even delve into the dynamics of organizational learning, the sine qua non of innovative enterprise in an industry such as biotech.

This type of analysis provides insights into the dynamics of relationships among the various actors in the drug development process. Of particular importance is the relationship of big pharma to biotech ventures through R&D contracts and alliances. The bargaining power of a biotech venture in its relations with big pharma will depend on such factors as the development of its core technology, its competencies in manufacturing compounds and performing clinical trials, and its access to venture capital and public equity markets for financing R&D. Over the course of the drug development process, the alliance relationship between big pharma and the biotech venture will be subject to early cancellation, ostensibly on the grounds on insufficient progress. Within the "innovative enterprise" analytical context, we can pose questions about the relation between productive performance and financial maneuvering in these R&D collaborations.

In the next section of the paper, we summarize four cases, two in the United States in Europe and two in Europe. In the United States, the case studies are Pharmacyclics founded in 1991 in Sunnyvale, California (near Palo Alto) and Myriad Genetics, founded in Salt Lake City, Utah in 1991. In Europe, the case studies are MorphoSys, founded in Martinsried near Munich, Germany in 1992, and Galapagos, founded in Mechelen, Belgium (between Brussels and Antwerp) in 1999.

3. Financial evolution of the biopharmaceutical firm: summaries of case-study research

Case Study 1: Pharmacyclics

Pharmacyclics was founded in 1991 based on the scientific collaboration between the company's co-founders, Jonathan L. Sessler, PhD and company ex-CEO, Richard A. Miller, MD. In the early 1980s Sessler, who was then a graduate student in chemistry at Stanford University, was treated for Hodgkin's lymphoma by Miller at Stanford University Medical Center. Based on scientific discussions between the two about novel therapies for cancer over the next several years, Sessler and his colleagues developed the "texaphyrin" molecules, so named because they were discovered at the University of Texas at Austin, where Sessler was a faculty member in the chemistry department. These molecules are used with radiation therapy to kill cancer cells. Pharmacyclics licensed the texaphyrin technology from the University of Texas (Brown, 2009). The third founder of the company, Stuart W. Young, brought his co-invention of diagnostic imaging technology from the University of Texas at Dallas. He became a vice-president of the company. The technology received FDA approval in late 1996 but the company could not market the product. In 1998, the most advanced drug candidate of the company based on texaphyrin reached Phase 3. Since then, the most developed texaphyrin drug, MGd, which had previously received fast track designation and orphan drug status (formerly named Gd-Tex and Xcytrin), was unable to gain market approval. Several FDA rejections precipitated the largest stock-price declines in the

company's history in 2001, 2006 and 2007. Currently Phase 2 clinical trials of the drug candidate are in process under the sponsorship of the National Cancer Institute.

Another major asset of the company is an in-licensing agreement. In 2006 the company acquired multiple small molecule drug candidates for the treatment of cancer and other diseases from a genetics company. Two of the four drug research programs of the company are now based on this license.

The company did its IPO in October 1995 when it only had a compound to be used in diagnostics submitted for FDA approval, while, of its various drug candidates, the most advanced was only in its Phase ½ clinical trials. Pharmacyclics' basic sources of finance have been public offerings and private placements of company stocks (see Table 4). The company has not generated significant revenues in its 20 years of operation.

Table 4. Key events in the evolution of Pharmacyclics

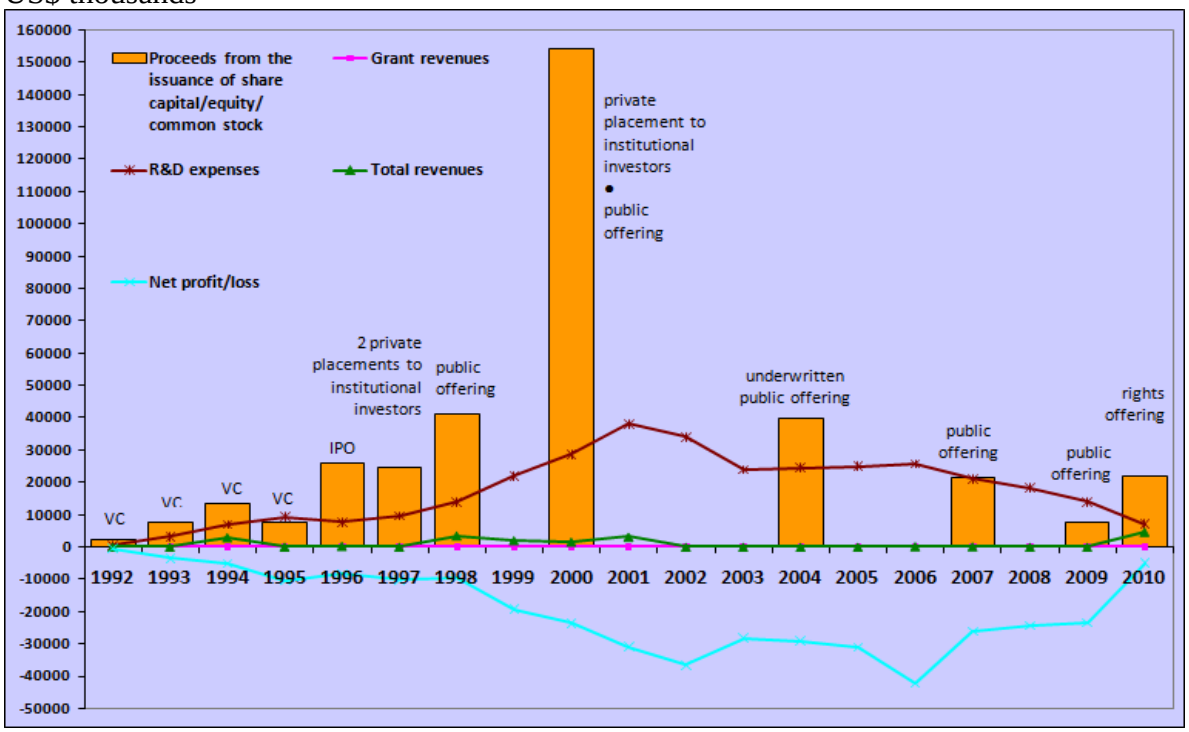
Type of event/finance	**Year(s)**	**Event/finance details**
	1991	Established in Sunnyvale CA
VC	1991-1996	Raised $31 million in funding from venture capitalists
IPO	October 1995	Raised $25.8 million in IPO and quoted on NASDAQ
Borrowing	December 2008 March 2009	Borrowed a total of $6.4 million from Robert W. Duggan
	June 2009	Transferred to NASDAQ Capital Market

In 2008 the founder and CEO Richard Miller left the company, and Robert Duggan, who had been a private venture investor, took control. Duggan had begun buying shares of the company in 2004, and he has been continuously acquired shares to the present. Moreover, in 2008 and 2009 the Company borrowed a total of $6.4 million from Robert W. Duggan & Associates.

In early 2009, the Phase 3 clinical research of the most advanced drug candidate failed again. The company experienced difficulties in getting Phase 3 data (Allison, 2008). As of May 2010, the most advanced drug candidate of the company is in Phase 2 clinical trials.

Since its inception, the company's major source of finance has been share issues (see Figure 4). The price per share issued has been highly volatile over time. The IPO price was $12 per share in 1995. The company sold its shares in a range of $0.93-$73.25 in nine offerings between 1997 and 2009. From its inception in April 1991 through December 2009, Pharmacyclics' total revenue has only been $18.7 million while the company had a total loss of $368 million. Sources of funds have been license, contract and milestone revenues, and small grants from SBIR and NIH.

Figure 4. Pharmacyclics finance and revenue recognition/expense, June 1991-December 2009
US$ thousands



Fiscal years end June 30th. 2010 values consist only of six months between July and December 2009.

Between 1991 and 1996, the company received several rounds of VC investment totaling $31 million. In its IPO, the company raised $25.8 million and continued to finance its activities through privately negotiated placements and public offerings. After the boom years in the early 2000s, stock market financing has become difficult for Pharmacyclics. Nevertheless it continued to sell its shares, mainly through public offerings with share prices lower than its IPO price. It also used or attempted to use other finance methods such as borrowing from the affiliate of its new CEO; rights offerings to investors, including the CEO; and a common stock purchase agreement with outsiders. As of December 2009, the company had only $5.8 million in cash.

Before the IPO, four venture capital funds held 50 percent of its shares and had representatives on the board of directors. Company founder Richard Miller owned around five percent of the company. After the offering, it took around three years for VC funds to exit, and in 1998, there was only one institutional investor with a share above five percent. Since then the holdings of institutional investors, especially hedge funds, have fluctuated sharply and have been short-lived. Today the only major individual investor is the company's new CEO, Robert Duggan. As of March 2010, he held 25 percent of the company's shares. At no time during its existence has the company attracted big pharma investment or any other major corporate investment.

The company also has received support from the National Cancer Institute (NCI, a division of NIH) for its biomedical applications and clinical research through Jonathan Sessler, a founder of Pharmacyclics who has been conducting his research at University of Texas at Austin in the name of Pharmacyclics. The company paid a total of $300,000 to the University for licensing in 1991. Over the period 1990-2009, Sessler received a total of $3.2 million from NCI for his research. Between 2004 and 2006, NCI also sponsored other Pharmacyclics' research worth $780,000. Moreover since 1997, NCI has sponsored clinical

trials of the company. As of 2010, the drug candidate MGd is still sponsored by NCI and its most advanced program is in Phase II. None of the NCI expenditures have been treated as capital investments in Pharmacyclics

The company's major source of revenue over its history has been partnerships, which have taken many different forms. The most important agreement was the one made in 1991 with University of Texas at Austin whereby Pharmacyclics secured licenses for several substances covered by UT patents while Sessler continued his research at UT on behalf of the company. In 1995, the company also in-licensed from two different electronics companies lasers and LED devices to be used in clinical trials. It entered two manufacturing agreements that were short-lived because of the cancellation of clinical research of related drug candidates. Its latest in-licensing partnership has been with a genomics company in an attempt to replenish its dried-up pipeline. The total cost of this partnership through the 2009 fiscal year has been $6.6 million, paid in cash and common stock. The partner is also eligible to receive royalty payments on annual sales of any drugs commercialized. In 2009 the company sublicensed one of its drug candidates based on this license. The $4.7 million that Pharmacyclics earned from this new partnership in 2009 is equivalent to one-fourth of its total revenue over 19 years.

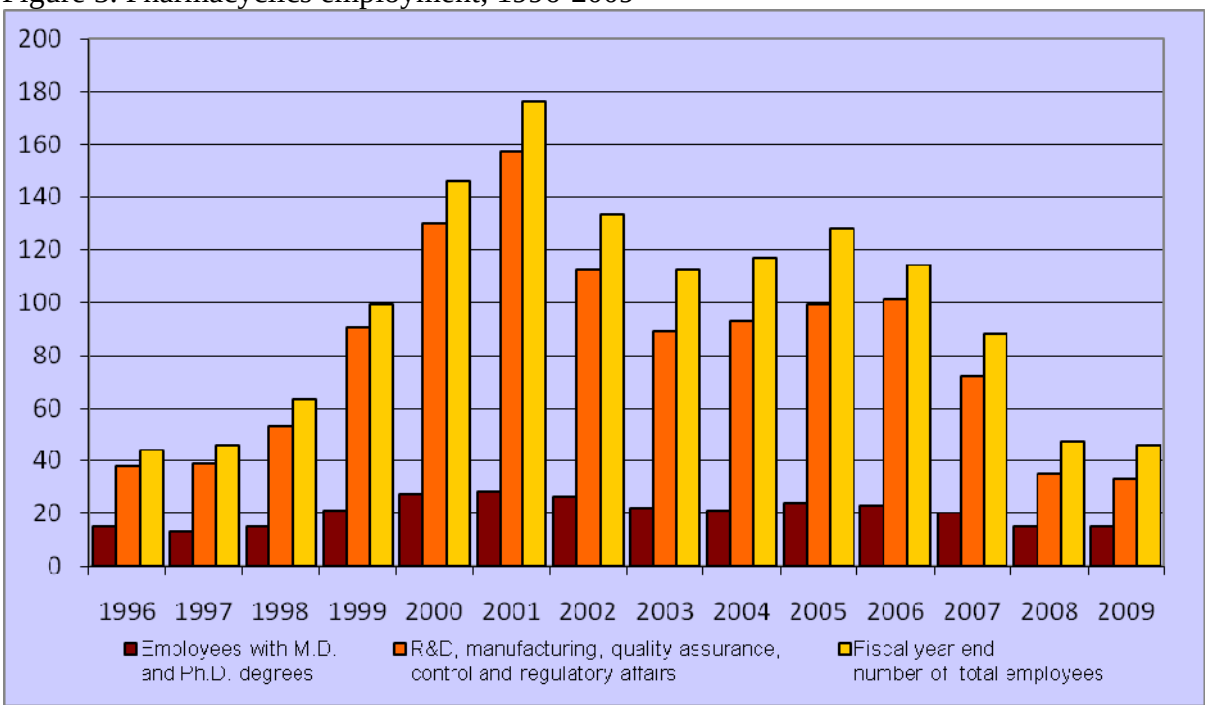
In 1997 NCI decided to sponsor the clinical development of several Pharmacyclics' drug candidates. It has mainly sponsored Phase 1 trials, and then passed the results to the company if the candidate was eligible for further trials. As of 2010 the company has two Phase 2 programs under sponsorship.

Pharmacyclics also formed three alliances for its early diagnostics technologies, which still remain to be marketed. Despite FDA approval of one product, the manufacturing and marketing partnership for it remained ineffective for several years, and was later terminated. During the same period the company also licensed another diagnostics technology to another company which failed to generate revenue. The company out-licensed two of its drug candidates to two different companies in 1997, but both drugs failed in Phase 2 clinical trials, and the agreements were terminated without generating substantial revenue.

Since its inception the company has had a total of 25 executives. There has been a moderate turnover in the executive committee but their titles have been continuously changing. Around three-quarters of the executives were hired from other pharmaceutical and biotechnology companies, and many of them have been medical doctors. As of 2010 none of Pharmacyclics' executive officers has more than five years of experience within the company.

Figure 5 shows the company's employment history. Up until 2001 there was a gradual increase in employment, as the company added personnel without MDs or PhDs. The company did substantial layoffs in 2002, and then employment remained stable until 2007. Another corporate restructuring occurred after the FDA rejection of a major product in early 2007. In mid-2009, the company's employment level was the same as it had been in 1996.

Figure 5. Pharmacyclics employment, 1996-2009



The compensation for officers and employees is composed of salaries, bonuses, benefits and stock options/convertible bonds. For executives, fixed compensation has been the major source of income. Even in the boom years, gains from exercising stock options were virtually non-existent. The option exercises that have taken place have occurred when executives have resigned from the company. When CEO and founder Richard Miller and 11-year CFO Leiv Lea resigned in 2008, they reaped a total of $1.8 million through option exercises. In several years the company also used bonuses as part of compensation but the failures of drug candidates put an end to them.

After the boom years of 1999-2001, the company's stock price has never reached its IPO level except for a very short period in early 2004 when the company did its last major public offering with a share price of $13. The company experienced huge stock-price declines repeatedly between late 2001 and early 2009 because of the failures of drug candidates in clinical trials and when, in March 2009, the company received notification from NASDAQ requesting a plan to achieve and sustain compliance with the continued listing requirements of the NASDAQ Global Market, including the minimum stockholders' equity requirement. During the period between November 2008 and April 2009, the stock price of the company was generally below $1. In June 2009, Pharmacyclics shares were transferred from the NASDAQ Global Market to the NASDAQ Capital Market.

Case Study 2: MorphoSys

MorphoSys was founded in Martinsried near Munich in 1992 by two chemists, Dr. Simon Moroney and Dr. Andreas Plückthun. Initially the company developed proprietary technology, based on academic work carried out by Prof. Plückthun at the Max Planck Institute of Biochemistry. In 1996 Pharmacia-Upjohn became MorphoSys' first commercial partner. From early 1994 several major venture capitalists injected $13.8 million into the company in advance of its IPO. In 1999 MorphoSys became the first biopharmaceutical company to be listed on the German stock exchange.

The early aim of MorphoSys was to establish its technology as the industry standard for antibody generation based on the most recent method of making antibodies. The technology was developed as part of the Human Genome Project, and augmented by a number of other technologies proprietary to MorphoSys including a screening technology and a method of generating high-quality peptide and protein libraries. Automation to achieve standardization and modularity was integral to the technology development process. The company collaborated with universities to develop its technology platform and to test potential therapeutic antibodies against cancer, inflammation and auto-immune disease targets. Today, using its HuCAL technology (the Human Combinatorial Antibody Library), MorphoSys develops antibodies which can be used in therapeutic research and diagnostics.

Since the early 1990s both MorphoSys and Cambridge Antibody Technology (CAT) have based their therapeutic antibody discovery technologies on phage display. In 1994 MorphoSys sought to restrict the scope of protection of CAT patents. The two companies engaged each other in a number of patent disputes that were eventually settled in 2002. Within the framework of the settlement, in August 2003 MorphoSys issued 588,000 shares to CAT and agreed to pay annual fees as well as future milestone payments in exchange of a license to the CAT patents related to HuCAL technology.

In 2005 MorphoSys made its first acquisition, the Biogenesis Group, bringing an additional source of revenue generation based on antibodies research. MorphoSys is now organized along different antibodies segment markets including custom antibody generation and contract manufacturing on behalf of customers.

To establish a platform for continuing growth, in January 2006 the company also acquired the Serotec Group, a major research antibody supplier in Europe. Serotec provides MorphoSys with a distribution network including subsidiaries and sales offices in the US and Europe (2005). AbD Serotec retains its own research and collaboration programs with its partners and customers in therapeutics as well as diagnostics.

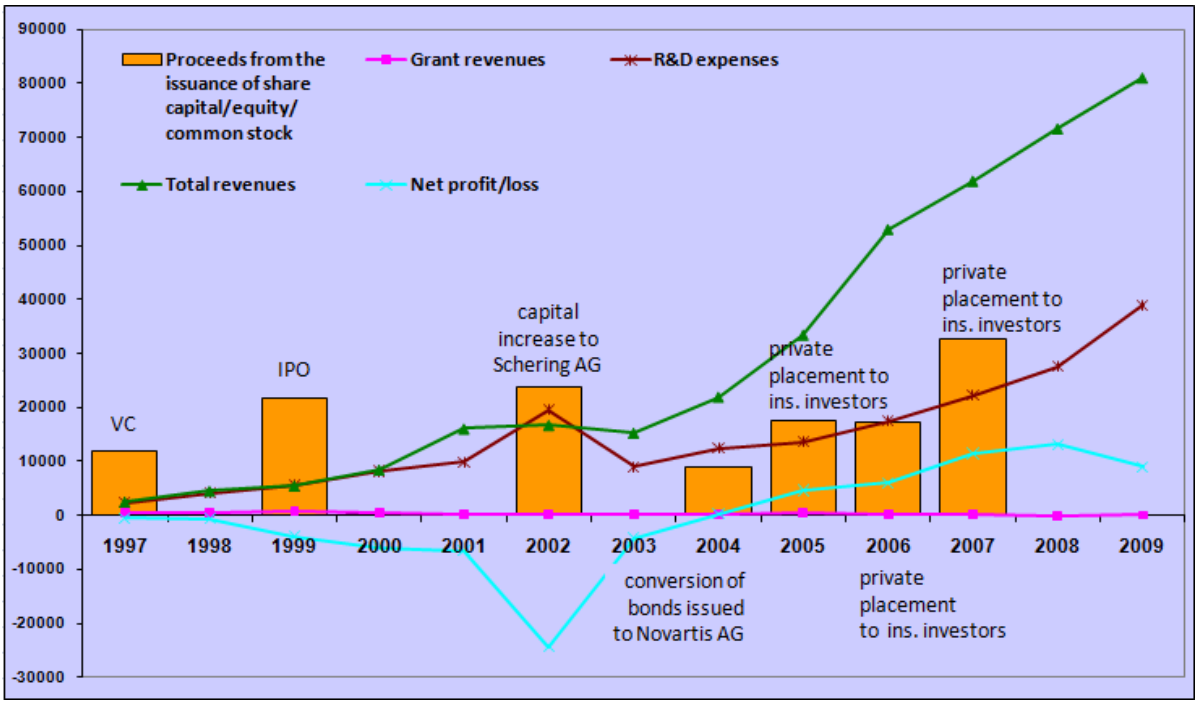
As shown in Table 5, MorphoSys' major sources of finance are public offerings, revenues from its strategic pharma alliances, and profits from access fees for its proprietary technology. The timeline below explains the funding history of the company plus other major events.

Figure 6 below shows the funding and revenue/expense history of the company. In September 1997 the company received $11.5 million in venture funding, in anticipation of an IPO one year later. Turmoil in stock markets in mid-1998 resulted in a six-month postponement of the IPO. After the IPO, the company raised money five times in ten years, mainly through the sale of stock to institutional investors. Grant revenues and licensing fees provided other major sources of revenues in the company's early years. For example, in 1995, the company received a $3 million grant from Bavarian Research Foundation for a joint project with Micromet GmbH. It continued to receive such regional grants in the following years. Over time grant revenues have become insignificant; they constituted 18 percent of revenues in 1997, but less than 0.1 percent in 2009. Research collaborations have resulted in increases in milestone revenues, while the two acquisitions in 2005-2006 have resulted in revenues generated through the company's antibodies segment.

Table 5. Key events in the evolution of MorphoSys

Type of event/finance	Year(s)	Event/finance details
	1992	Established in Martinsried/Munich, Germany
VC	1994-1997	Raised $13.8 million in funding from venture capitalists
Grant	May 1995	Received a $3 million grant from Bavarian Research Foundation with Micromet GmbH
Debt	Up to 1999	Accumulated a long-term debt of DM 6.2 million with Silent Partnerships
IPO	March 1999	Raised €25.8 million in IPO and quoted on Neuer Markt; the first German biotechnology company to go public
Build up	February 2000	Founding of MorphoSys USA Inc,; closed November 2002
	April 2000	MorphoSys AG admitted in "Dual-Trading" to EASDAQ
Build up	November 2002	Formation of MorphoSys IP GmbH s to administer internally generated intellectual property
	January 2003	Admitted to Prime Standard segment of Frankfurt Stock Exchange
M&A	January 2005	Acquired Biogenesis Group
M&A	January 2006	Acquired Serotec Group

Figure 6. MorphoSys finance and revenue recognition/expense, 1997-2009
€ thousands



In 2009 MorphoSys derived 76 percent of its revenues from funded research, licensing fees and milestone revenues while the AbD Serotec segment generated 24 percent of total revenues. Beginning in 2003 revenues increased faster than R&D expenditures. Despite the absence of drug revenues, the earnings of the company substantially increased as the result of licensing and partnering activities as well as services. The geographical distribution of revenues also changed substantially over the years. In 2002 the US market generated 76 percent of revenues while the rest came from Europe. In 2009 North America accounted for

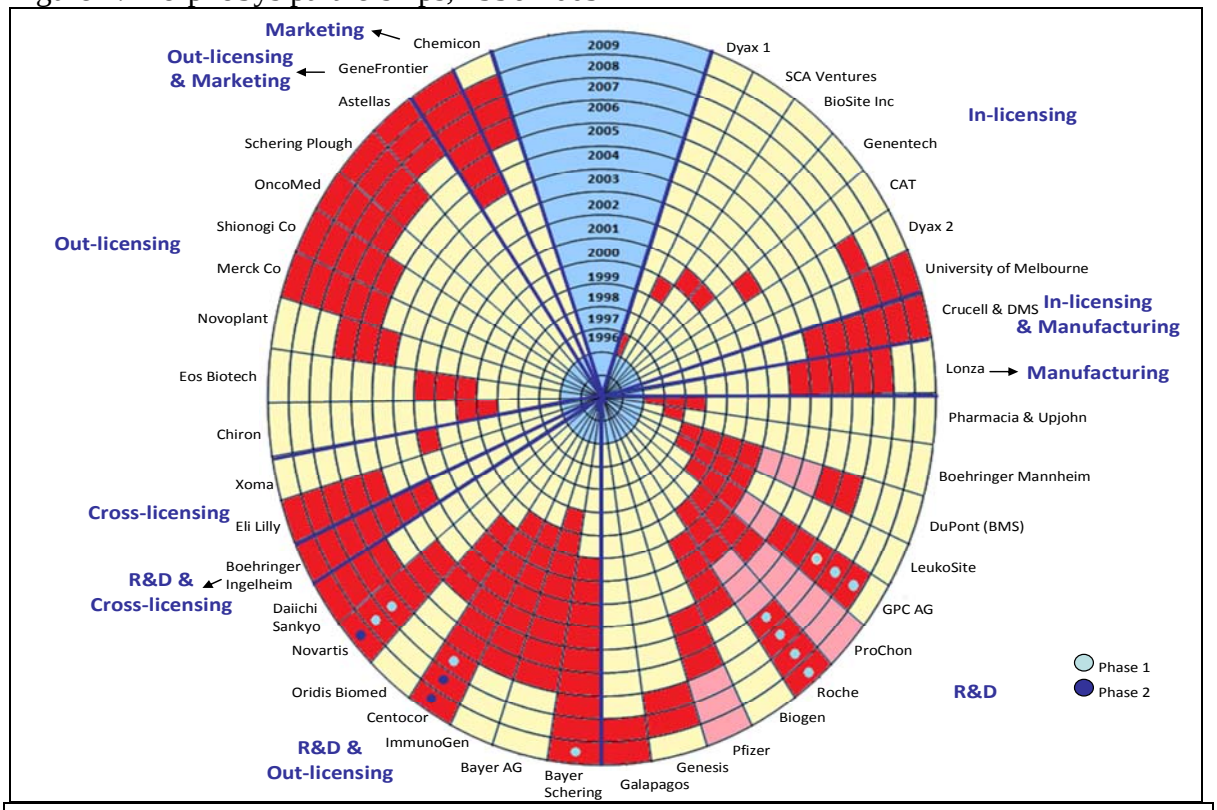
only 18 percent of revenues with the other 82 percent from Europe and Asia (Japan). As a European company the geographical expansion of its activity has been striking. The company has had positive net income since 2004.

The company paid a total of €36.3 million for two acquisitions, with €27.5 million paid in cash and the rest through the issuance of new shares. In 2007 the company decided to purchase its own shares when necessary. The purposes include redemption, fulfillment of conversion and option rights and usage as acquisition currency in different contexts. The decision has been repeated in 2008 but the company has not performed any repurchases.

Ownership of the company has changed substantially since its inception. After the IPO in 1999, share ownership by venture capital stakeholders declined from 65 percent at the Company's IPO in March 1999 to less than 20 percent in December 2000. After the fluctuations of ownership between 1999 and 2001, big pharma capital investment flowed in through the R&D alliances. The ownership of insiders gradually decreased, leaving them with only two percent of the company shares currently.

Figure 7 depicts the partnership activity of the company since 1996. The scale and scope of many of the partnerships has extended or expanded over time. In-licensing partnerships are generally single-round agreements to license patents or working technologies of other companies. MorphoSys makes payments to its partners depending on the content of the agreement. In-licensing can be enlarged by upgrading existing technology licenses or including other types of agreements related to the existing partnership such as manufacturing.

Figure 7. MorphoSys partnerships, 1996-2009



Red and pink areas indicate active and dormant years of collaboration respectively. Yellow areas indicate non-collaborative years.

R&D partnerships, which have been the company's major sources of income, generally aim to develop drugs with partners if they achieve success at research and preclinical development stages. By 2009 the company has four R&D partnerships with seven drugs in the clinical development stage. In R&D partnerships with out-licensing, the company also provides its partners with access to its core technology.

As an important source of income, the progress of these R&D activities is critical to the company's financial condition. The pink cells represent the dormant years of the partnerships (that is, years without any new information about the collaboration). Several of those partnerships have been dormant because either the partner did not begin new projects under the agreement or did not progress in its research. For MorphoSys, any slowdown of partners in the development of its drugs means less current income because of the lack of milestone payments as well as the postponement of any future income expected from the drug.

R&D partnerships accompanied with out-licensing of the company's technology do not have dormant years as the company receives regular access fees. MorphoSys's most important partnership, with Novartis, is in this category. Few of those R&D partnerships also include share acquisitions by partners as important sources of finance in addition to R&D and licensing revenues. The company has also formed cross-licensing collaborations after the resolution of patent disputes with counterparts, out-licensing partnerships for its proprietary technology, and collaborations to increase marketing opportunities of its main technology.

As an example of the duration of time over which these partnerships must persist to have the chance of developing a successful drug, the collaboration with Roche on Alzheimer's disease, began in 2000. A clinical trial of a drug for this disease lasts at least two years; in this case drug development has been in Phase 1 for the last four years. It is unlikely that a successful drug can come to the market before 2015. Moreover as a risk dispersion strategy, Roche currently has five different drug development programs on Alzheimer's disease including two antibodies (one with MorphoSys and one within Genentech) and three non-biotech, small molecules (two within Roche and one within Memory Pharma). Four of them are in Phase 1 while the one within Memory Pharma, a branch of Roche, has reached Phase 2. MorphoSys is much more dependent on Roche's commitment to their partnership than vice versa.

With all of its partnership activity, MorphoSys has had a continuous increase in its workforce since the inception of the company. Especially after its acquisitions, the number of non-R&D employees has increased rapidly. More generally, the company has had an increasing interest in service activities.

Since its inception the company had a total of only five executives for four positions (CEO, CFO, Chief Scientific Officer, and Chief Development Officer), Except for the CEO, the executive committee is composed of people with prior experience with pharmaceutical companies. Their compensation has been composed of salaries, bonuses, benefits and stock options/convertible bonds. With the exception of 2007, since 2005 stock options have been an important source of income for executives. As of 2009, 56 percent of total executive compensation was composed of the gains from stock and convertible bond exercises.

The company did its IPO right before the boom years for technology firms, with its stock price fluctuating in a range of €6-€120 between early 2000 and late 2001 without any major event specific to the company. But since early 2005 its stock price has remained stable, and the recent crisis has not had any effect on its general trend. Although the company has not

obtained any finance capital since May 2007, its cash flow has remained stable due to its rising revenues.

Case Study 3: Myriad Genetics[4]

Myriad Genetics Inc. was founded in 1991 based on the collaboration between the company's co-founders: Mark H. Skolnick who has a PhD in genetics and a BA in economics and Peter D. Meldrum who was the head of a biotech-focused venture capital group and had a BS in engineering. In 1992 Walter Gilbert, a Nobel laureate for his contributions to the development of DNA sequencing technology and a founder and early CEO of Biogen, joined the company as a founding scientist. Based on the academic collaborations with University of Utah, the company was involved in the discovery of BRCA1 and BRCA2, breast and ovarian cancer predisposing genes.[5] In 1996, it introduced the first diagnostics product based on this research – the BRACAnalysis test for women who have been diagnosed with breast or ovarian cancer and women who are at risk for hereditary breast and ovarian cancer. The development of therapeutic products for the treatment and prevention of major diseases associated with these genes has been the second important commercial strategy of the company.

The company claims that its major strategy is to seek patent protection in the United States and major foreign jurisdictions for genes, proteins, antibodies, diagnostic markers, technologies, methods, processes and other inventions which it believes are patentable and useful in the development or analysis of molecular diagnostic products. By 2009 the company owned or had licensed rights to 213 issued patents as well as numerous patent applications in the United States and foreign countries. Unlike the competition based on product innovation among drug firms, Myriad's diagnostics services products put it in competition with other diagnostics firms or healthcare providers in terms of quality, rapidity and affordability of its services. Its emphasis on intellectual property is not only to protect its own patents but to discourage others to patent similar technologies:

> Others may obtain patents having claims which cover aspects of our products or processes which are necessary for or useful to the development, use or performance of our diagnostic products. Should any other group obtain patent protection with respect to our discoveries, our commercialization of potential molecular diagnostic products could be limited or prohibited (Myriad Genetics 10-K, 2009, 6).

Myriad did its IPO in October 1995 without any marketed product. It had drug candidates in early periods of R&D but the focus of the company was on its diagnostics technologies. Until the spin-off of its therapeutics business completed in 2009, the company only had four drug candidates, one in Phase 2 and the rest in Phase 1. In its early years, R&D contracts accounted for most of the company's revenues. Since 1996, however, the company has launched seven molecular diagnostic products for assessing a person's risk of developing various cancers and optimizing dozes in ongoing cancer therapies. In fiscal 2009 it generated a total of $326.5 million in diagnostics revenues. In 2002, the company had a 50-50 ratio in

[4] Preliminary research on Myriad Genetics can be found in Liu 2010.

[5] Myriad Genetics' monopoly over BRCA1 and BRCA2 diagnostics tests, as a result of its US patents, has been the subject and considerable controversy and litigation. See Cassier and Gaudillière 2000; Sevilla et al. 2003; Orsi and Coriat 2005; Orsi et al. 2006; Gold and Carbone 2008; Löwy and Gaudillière 2008; United States District Court 2010.

its product and research revenues. After the therapeutics spin-off in early 2009, diagnostics sales became the single source of revenue for the company.

To date, the major sources of the company's finance have been the private placements and public offerings of its shares. For the period between its inception in May 1991 and its first major private placement in July 1995, it accumulated a deficit of $9 million. The first equity investment into the company came in August 1992 from Eli Lilly and its former subsidiary, Hybritech, through research and license agreements. Between February 1995 and September 1995, Myriad received a total of $25 million through three private placements (see Table 6). The last two were based on research agreements with two pharmaceutical firms, Ciba-Geigy and Bayer. Less than a month after the $10 million equity investment of Bayer, the company did its IPO on October 5, 1995 and raised a net of $49.2 million. To the present, the company has raised close to $530 million from the stock market through private placements to pharmaceutical companies and institutional investors, and through public offerings. Since 2003 the only source of equity investment has been the public offering.

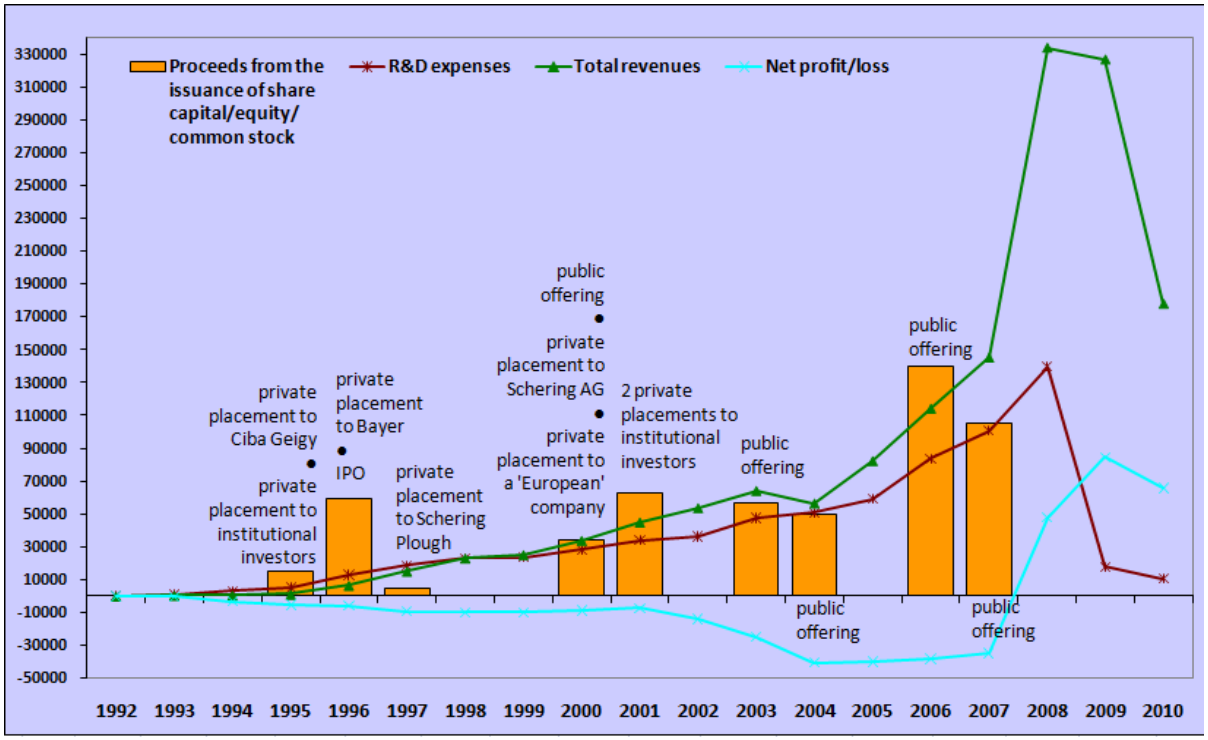
Table 6. Key events in the evolution of Myriad Genetics

Type of event/finance	**Date**	**Event/finance details**
	1991	Established in Salt Lake City, UT
Private placement	1995	Raised $25 million in funding through private placements
IPO	October 1995	Raised $49 million in IPO and quoted on NASDAQ
Build up	April 1999	Formed Myriad Pharmaceuticals Inc. to develop lead therapeutic compounds
Build up	April 2001	Formed Myriad Proteomics, Inc. with Hitachi Ltd. and Oracle Corporation to map the human proteome and market it to pharma and biotech companies
Spin-off	June 2009	Completed the spin-off of Myriad Pharmaceuticals Inc.

Figure 8 shows the finance and revenue/expense history of Myriad Genetics since its inception. It did not receive any capitalized government funding during the period while Skolnick, the founder of the company continued his research at University of Utah, funded by NIH. Through the end of fiscal 2007 it had a cumulative net loss of $250 million. For the two and a half years between June 2007 and December 2009, however, it generated a net income close to $200 million. In fiscal 2008, the company recorded research revenue of $100 million through a drug development agreement with Lundbeck. In 2009, however, it transferred its drug development business with a capital contribution of $188 million to its spin-off Myriad Pharmaceuticals. After the spin-off, research and development expenditures of the company decreased from $140 million to $18 million for fiscal 2009.

Figure 8. Myriad Genetics finance and revenue recognition/expense, June 1991-December 2009

US$ thousands



Fiscal years end June 30th. 2010 values consist only of six months between July and December 2009.

Since its IPO, the company has attracted small slices of investments from hundreds of investors including pension, mutual and hedge funds as well as large ones from more than 15 institutional investors with ownership stakes above five percent of total outstanding shares, maintained generally over 2–3 year periods. One particular investment was Bayer's $10 million equity infusion just weeks before the IPO, most probably designed to help boost the IPO stock price. Bayer maintained its stake until the boom year of 2000. In August 1996 the three founders of the company held a total of 1.3 million shares for a 15 percent stake. As of August 2009 they had around 3.2 million shares for a 3.3 percent stake. On the same date, a total of 17 executive officers and directors had a 7.3 percent stake in the company.

As a major strategy to generate revenue, especially before the product launch, the company formed alliances with pharmaceutical and multinational firms, and universities. These included, among others, research and license agreements with several pharmaceutical and other companies including, Eli Lilly (1992), Hybritech (1992), Ciba-Geigy (1995), Bayer (1995), Schering-Plough (1997), Schering AG (1998), Pharmacia (1998), Novartis Agricultural (1999), Roche (1999), Hitachi (2000), Oracle Corporation (2001) Abbott (2002), Pharmacia (2002), Salmedix (2005) and Lundbeck (2008). These agreements include drug development research collaborations, in-licensing patents and technologies of partners, and out-licensing genomics sequencing technologies and bioinformatics expertise. The company’s collaboration with Lundbeck granted this Danish company certain marketing rights for the therapeutic candidate Flurizan, which was under Phase 3 clinical trials at the date of the agreement. Lundbeck paid Myriad a $100 million non-refundable fee. In the following month the drug failed, and Myriad discontinued all Flurizan development activities.

As early as 1991, the company made a number of collaborative agreements with the University of Utah pursuant to which the company was granted an exclusive, worldwide license to the University's patent rights arising out of the discovery of the BRCA1 breast and ovarian cancer gene for use in the diagnosis and treatment of breast cancer. This licensing agreement was followed by others based on partnered research on MTS1 and BRCA2 cancer predisposing genes. During 1995 another license agreement with University of Utah granted the company worldwide rights to use the database of families, clinical information and DNA samples for the discovery of genes for the diagnosis and treatment of cardiovascular disorders and obesity. In 1996 the company also made a patent and technology license agreement with the University of Texas in connection with research directed to the isolation sequencing and characterization of genes involved in leukemia, pursuant to which the company was granted a worldwide license to any commercial application of leukemia genes discovered during such research. Myriad continued to seek patents related to its diagnostics business and in-licensed many of them from other universities and research centers which are not mentioned here. The company transformed several of these licenses into commercial diagnostics products.

Lastly, Myriad entered into various reimbursement and marketing collaborations in the United States with Aetna, Blue Cross, and Labcorp among others. It also signed agreements with partners from Canada, Europe and Japan to ensure the sales of its products.

Especially after the launch of its diagnostic products, the growth of Myriad's workforce has been remarkable. In 1996 (the earliest year for which publicly available workforce information is available), the company had a total of 181 employees including 27 people holding doctoral degrees. Right after its first product was marketed in 1997, it hired an army of sales and marketing personnel. As a result PhDs and MDs became a diminishing proportion of the total workforce. In 2008, the year before the spin-off of Myriad Pharmaceuticals, the company had 994 employees of whom 108 held PhD or MD degrees. After the spin-off, the number of employees decreased to 869, of whom only 35 employees held PhD or MD degrees. With the related decrease of R&D expenditures between the two years, Myriad Genetics became primarily a company dedicated to the marketing of its proprietary technology.

Since its inception the company had a total of 18 executive officers, with a moderate turnover in the executive committee (see Table 7). More than half of the executives were hired from other pharmaceutical and biotechnology companies. Currently the committee is composed of six people, all of whom have at least eight years of experience within the company.

Executive compensation has been composed of salaries, bonuses, other benefits and stock options. Public US companies are obliged to publish the compensation of the CEO and other four highest paid executives. Figure 9 shows the levels and sources of compensation of Myriad's highest-paid executives since 1995. As can be seen, large increases in executive compensation have depended on the gains from exercising stock options, which in turn depend on a booming stock price. In fiscal 2001, the value realized through stock option exercises of only the top five executives exceeded $16 million. This amount was above $23 million in fiscal 2009. In recent years bonuses have also became an important source of executive compensation.

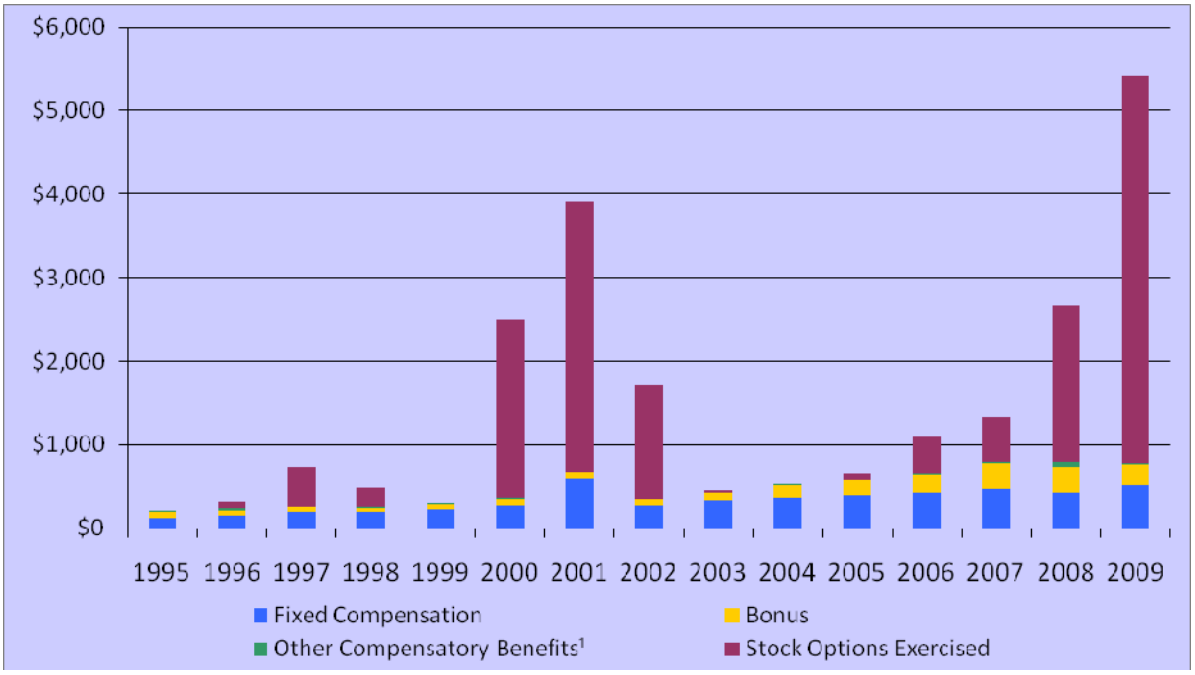
Table 7. Executive officers of Myriad Genetics since 1991

Name	**First Position in the Committee**	**Entry Year***	**Exit Year**	**Previous Employer**
Peter D. Meldrum (f)	CEO	1991	-	CEO of Founders Fund, a biotech-focused VC group
Dr. Mark H. Skolnick (f)	VP of Research and Development	1991	2010	University of Utah
Jay M. Moyes (a)	CFO	1993	2007	CFO of Genmark, an agricultural biotech company
Janet H. Haskell (a)	President, Myriad Genetic Lab	1995	1998	VP and General Manager of SmithKline Beecham Corp
Dr. Arnold Oliphant (p)	VP Research, Functional Genomics	1995 (1996)	2000	Director, an agricultural genetics company
M.D. Gregory Critchfield (a)	President, Myriad Genetic Lab	1998	2010	VP, Chief Medical & Scientific Officer of Quest Diagnostics
M.D. James S. Kuo (a)	VP of Business Development	1998	2000	CEO of Discovery Labs, a biopharmaceutical company
Dr. Adrian N. Hobden (a)	President, Myriad Pharmaceuticals	1998	2009	Director, Global Biotechnology Ventures with Glaxo Wellcome
Christopher L. Wight (p)	VP, General Counsel	1998 (1999)	2002	Director of Intellectual Property at Immunex Corporation
Dr. Sudhir R. Sahasrabudhe (a)	VP, Research and Development	2000	2002	Director of U.S. Biotechnology with Aventis Pharmaceuticals
S. George Simon (a)	VP of Business Development	2000	2007	VP, Corporate Development with MorphGen, a biopharmaceutical company
William A. Hockett (p)	VP of Corporate Communications	1993 (2001)	2009	Marketing Manager for Diagnostic Products Corp
Dr. Jerry S. Lanchbury (a)	VP Research	2002	-	GKT School of Medicine, King's College
Richard M. Marsh (a)	VP, General Counsel & Secretary	2002	-	Director of Intellectual Property of Iomega Corporation
W. Wayne Laslie (a)	COO, Myriad Pharmaceuticals	2004	2009	CEO of Cappharma Services, a pharmaceutical marketing & consulting firm
James S. Evans (p)	VP Finance	1995 (2005)	-	KPMG, LLP
Mark C. Capone (p)	COO, Myriad Genetic Lab	2002 (2006)	-	Product Development Manager of Eli Lilly
Robert G. Harrison (p)	Chief Information Officer	1996 (2008)	-	n/a

f=founder; a=appointed to executive committee on entry; p=promoted to executive committee from within
* Year in parenthesis reflects the year of promotion to the executive position

Figure 9. Myriad Genetics, average total compensation and it components, highest paid executives, 1995-2009

US$ thousands

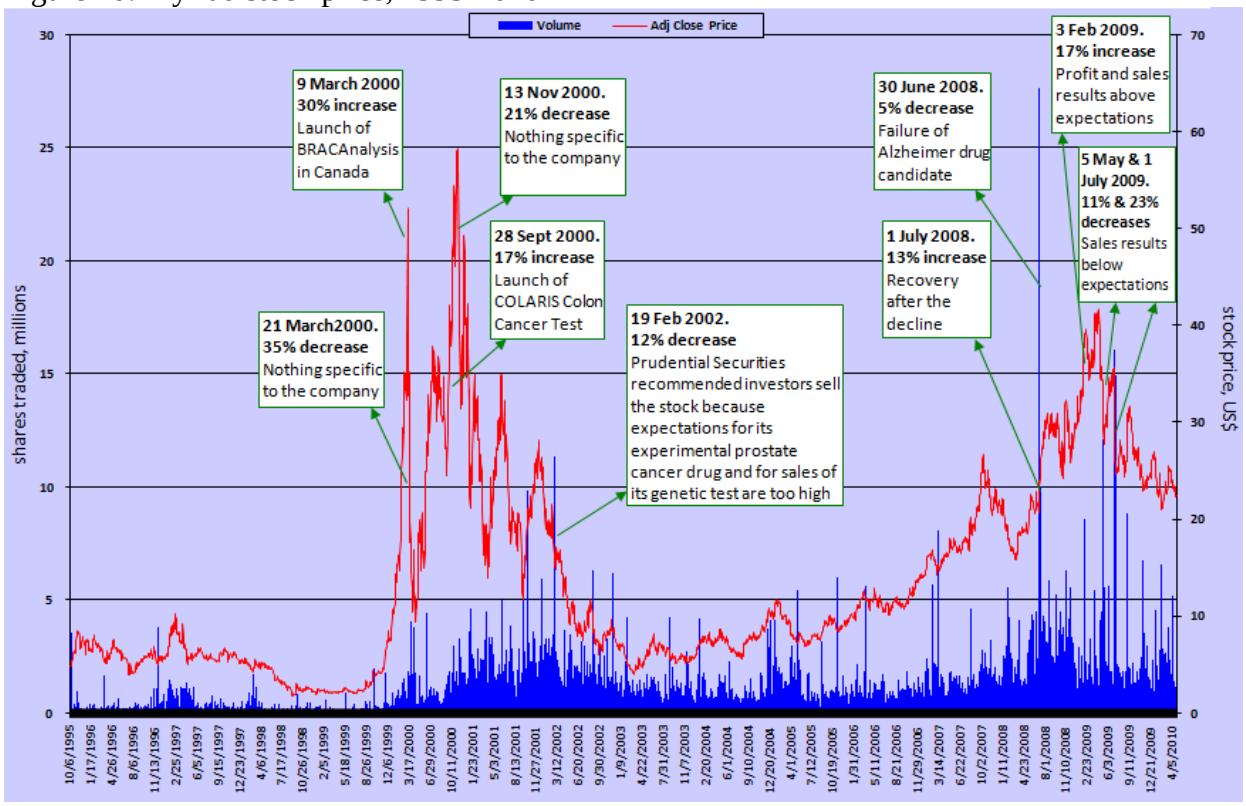


Top three in 1995, top four in 1996 and 1997 and top six in 2008.

[1]Include life insurance payments, 401(k) contributions, and a resignation-agreement payment for 2008

Figure 10 shows the changes in Myriad's stock price. During the boom years of the early 2000s, the stock price of the company rose rapidly with events such as product launches or fell for no apparent reason. In the recent boom period of 2008-2009, the fluctuations have been driven by revenue expectations of investor analysts. Interestingly, patent disputes, including the most recent court decision invalidating seven patents of the company related to breast and ovarian cancer, have not created significant downward pressure on the company's stock price. Moreover, there was a stock price increase in July 2008 after the failure of Alzheimer drug candidate collaboration with Lundbeck, probably because of the upfront non-refundable $100 million fee that Lundbeck paid to the company.

Figure 10. Myriad stock price, 1995-2010



Source: Yahoo! Finance

Case Study 4: Galapagos

Galapagos was founded in 1999 in Mechelen Belgium (located between Brussels and Antwerp) as a joint venture of two other biopharmaceutical companies, Crucell and Tibotec. The two founders, Rudi Pauwels and Dinko Valerio are both scientists who have been in the biotech business since the early 1990s. From the beginning, Galapagos has operated as a hybrid business model, combining internal discovery programs with service activities. Their collaboration was the result of an IntroGene (now Crucell) program to use adenoviral technology for functional genomics applications and Tibotec's robotics and data management capabilities which enabled the development of a high-throughput target discovery and validation platform.

Thus the major technological capability of the company is to develop novel drug targets for novel drug candidates, mainly in bone and joint diseases. Early work developed the company's proprietary technology and target discovery platform based on the licenses acquired from Crucell and Tibotec. In the early 2000s the company established a number of collaborations with research institutes such as Netherlands Cancer Institute and Flanders Interuniversity Institute for Biotechnology as well as other companies to identify and validate novel targets for therapies in the very early stages of drug discovery.

Galapagos did its IPO in May 2005, and is quoted on Euronext Brussels and Amsterdam. Shortly after the IPO, the company started to do acquisitions to build its drug discovery capabilities. Through March 2010, it acquired five companies with different technological and organizational capabilities. Acquisitions also brought new sources of revenue.

The company's major business strategy is to strengthen and complement "a balanced and well-filled" pipeline by selectively acquiring candidate drugs. Firstly, it directly addresses a knowledge accumulation process of drug development comprised of material technology development, expertise development and business development. Secondly it helps companies attract more capital through partnerships. For Galapagos, acquisitions complement partnerships as it balances the company's proprietary programs and R&D alliances in developing its pipeline. The company now operates in seven countries.

Table 8 outlines Galapagos' funding history. Currently, its major sources of finance are public offerings, revenues from its service activities, and strategic pharma alliances.

Table 8. Key events in the evolution of Galapagos

Type of event/finance	**Year(s)**	**Event/finance details**
	1999	Established in Mechelen Belgium
VC	2002-2003	Raised $31.1 million in funding from venture capitalists
Grant	2002	Received grants for a total of €5.2 million from IWT
IPO	May 2005	Raised € 22.4M in IPO and quoted on Euronext Amsterdam and Brussels
M&A	October 2005	Acquired BioFocus plc a company previously listed on the London AIM through an all share offer
M&A	July 2006	Acquired Discovery Partners International with a price of €4.25 million paid in cash
M&A	December 2006	Acquired Inpharmatica Ltd. through an all-share transaction
M&A	December 2006	Acquired ProSkelia SASU (afterwards renamed Galapagos SASU) in exchange for new shares with the effect that the net consideration did not include any cash
Grant	October 2007	Awarded €5.2 million in research grants of Dutch government and EU
Grant	January 2008	Awarded €4.4 million grant for rheumatoid arthritis drug development of IWT
	April 2008	Quotation on AIM was cancelled
Sale	November 2008	Completed the sale of its San Diego based affiliate of BioFocus DPI
M&A	February 2010	Acquired Argenta Discovery 2009 Ltd. with a price of €16.5 million paid in cash

Figure 11 shows the funding and revenue/expense history of the company. Up until its IPO, its activities were mainly financed by venture capital investment, government awards and research collaborations. After its IPO, the company proactively used its stock as a source of finance along with cash to do acquisitions. It raised money through private placements to institutional investors as well as big pharma four times in four years between 2006 and 2009.

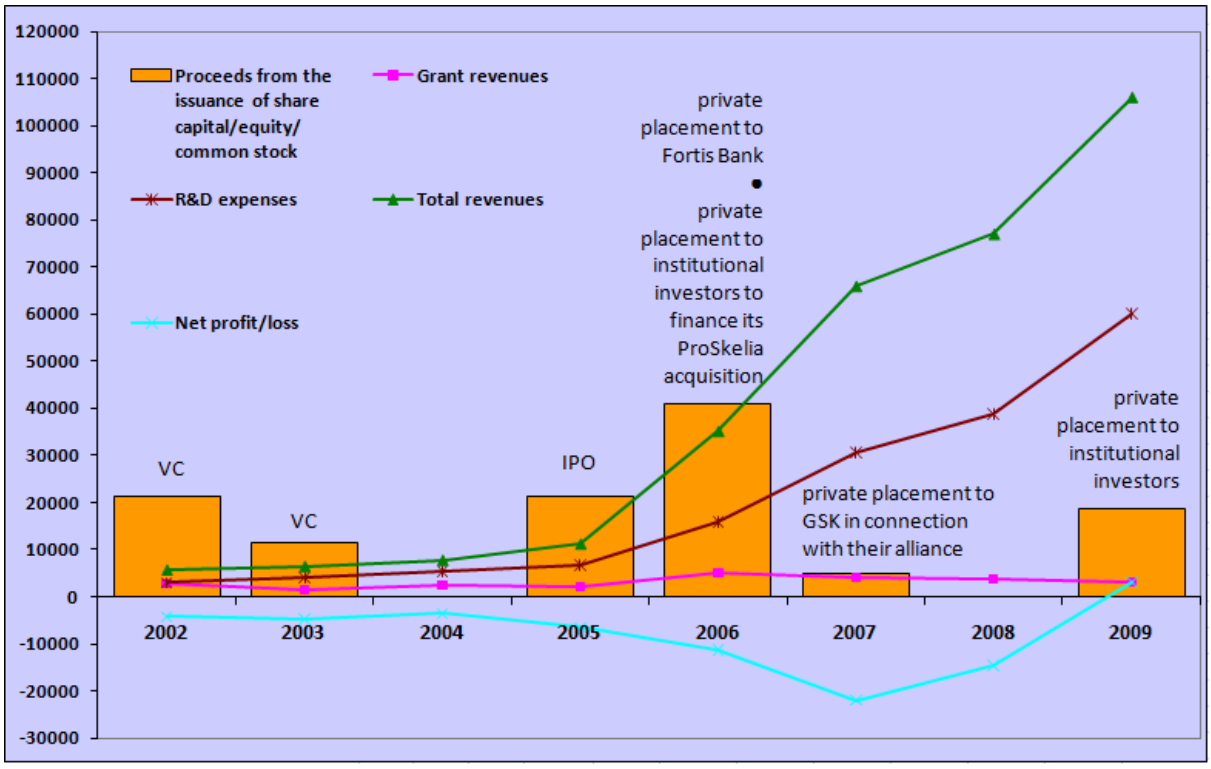
With the help of its acquisitions, the company rapidly increased its revenues. By 2009 service revenues generated by BioFocus DPI made up 54 percent of Galapagos' total revenue. Including the BioFocus DPI sales, 76 percent of total revenue came from R&D contracts and milestones. The company did not report the geographical distribution of its revenue in 2009,

but in 2008 it had a 29 percent in the UK, 57 percent in the rest of Europe, and 14 percent in the United States.

Since 2002 R&D grants from the Flemish Institute for the Promotion of Industrial Scientific-Technological Research have been an important source of Galapagos' revenues. The Flemish Institute supports drug discovery and development efforts of the company including clinical trials. The company also has various research and supply agreements with several governmental and non-profit organizations including Netherlands Institute for the Stimulation of Technological Development and Collaboration, Dutch Ministry of Economic Affairs, High Q Foundation, Institute for OneWorld Health and NIH among others. Some part of the revenue out of these agreements takes the form of non-refundable grant revenue.

In 2007, the company declared a program to purchase its own shares subject to the availability of sufficient retained earnings or profit reserves. The program has been repeated in 2009 but the company has not done any repurchases. In 2009, for the first time, the company had positive net income.

Figure 11. Galapagos finance and revenue recognition/expense, 2002-2009
€ thousands

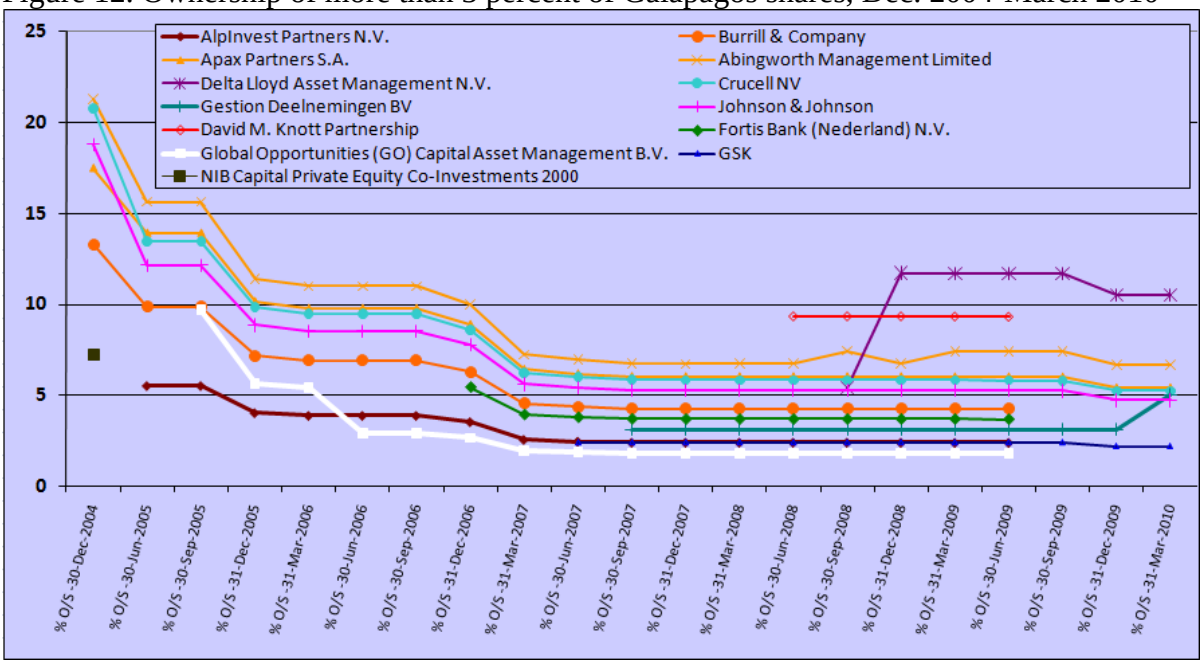


The funding received through venture capitalists totaled $31.1 million between 2002 and 2003. Since the IPO in 2005 two of the early venture capitalists exited completely (one immediately after IPO, the other in mid 2009), but two other early venture capitalists have maintained their stakes. Founding companies also kept some shares, although their combined ownership stake decreased from 40 percent in 2004 to 10 percent in 2010. Other than founding companies, the only big pharma investment came through GSK in 2007.

As shown in Figure 12, the most interesting observation concerning the evolution of ownership of the company is its stability. Both venture capitalists and founding companies

have maintained their stakes. This stability in ownership is quite unusual for biotech companies, especially when compared with their counterparts in the United States.

Figure 12. Ownership of more than 3 percent of Galapagos shares, Dec. 2004-March 2010



Source: Thomson Reuters and company reports

Galapagos' partnerships take two forms: R&D alliances mainly with big pharma and service agreements mainly performed by BioFocus DPI. Besides generating revenue, BioFocus adds value to ongoing R&D programs, whether they are internal or collaborations. To date Galapagos and its service division have formed more than 70 partnerships and more than ten of them have been R&D alliances with pharmaceutical and biopharmaceutical companies. For example in 2006, Galapagos signed its first major R&D alliance with GSK to discover drugs for osteoarthritis. This alliance is still active, and the company has earned €46 million in payments to date. Galapagos also has research collaborations with government and non-profit organizations.

Since 2006 the company has accelerated licensing agreements with big pharma to generate more revenue. The company continues its research on bone and joint diseases either solely or with alliances. In 2009 it acquired Nanocort® to complement Galapagos' R&D program in rheumatoid arthritis with a smaller private company that will receive a minority share of future revenues from the commercialization of the drug. The company has developed novel approaches to bone and joint disease research with an equally distributed alliance with MorphoSys. In addition the company supports it pipeline with novel areas of research including cachexia (again from ProSkelia), infections, inflammations and Alzheimer.

Galapagos, therefore, has been diversifying the development of its capabilities rather than running the risk of focusing only on a specific area. The company describes its alliances in these diverse fields as 'strategic'. It continuously extends and expands its partnerships to ensure money inflow through enlarged R&D activity, thus also mitigating the risk of failure.

The growth of Galapagos is also reflected in the development of its workforce. Until 2005 its headcount remained modest but with acquisitions the number of employees increased rapidly. As of 2010, the workforce is slightly above 500, with about 250 of them working on R&D.

Since its inception the company had a total of 14 executives from a wide range of European companies. The CEO is an ex-Crucell director who has been in charge since the beginning. Executive compensation consists of salaries, bonuses, benefits and stock options (warrants). In 2007, of a total of 325,000 options that had been granted to executives at the beginning of the year, 126,000 were exercised by the end of the year. Between 2005 and 2008, 10 to 15 percent of the total options granted to the entire workforce were exercised. In late 2009 the company began to publish press releases about executive option exercises.

Since its IPO, stock price of the company fluctuated in a range of €2.8-11.5 as it has been affected by the financial crisis. Beginning in 2009, stock prices started to rise again and transaction volume has also increased after new offerings.

4. The impacts of financial institutions on innovation and inequity: preliminary observations

Pharmacyclics had early success in quickly bringing its drug candidates to the later stages of clinical trials as well as in out-licensing its diagnostic technologies developed by the founders. In its early years, equity markets helped the company develop its drug candidates based on the research funded by NCI. But after the downturn of 2002, equity finance dried up, and the company started to look for other options to develop its pipeline and finance ongoing R&D efforts. In the 2000s Pharmacyclics struggled with the repeated failures of its advanced drug candidates. The company could no longer secure an adequate supply of venture capital and public equity investment through private placements. Lacking new R&D contracts and milestone payments, Pharmacyclics was sustained by public offerings of gradually decreasing amounts as well as NCI funding of clinical trials and university research on behalf of the company. Ownership of the company has been neither stable nor correlated to its value creation efforts. Moreover the ex-CEO and ex-CFO left the company in 2008 with a total of $5.7 million in compensation and severance payments, including stock option exercises. The company had only $5.8 in cash at the end of 2009.

Founded one year after Pharmacyclics, MorphoSys was unable to mobilize substantial finance in its early years for the rapid development of its drug candidates. By 2004, after 12 years of existence, the company still did not have any candidate in clinical trials. Other than funds raised in its IPO in 1999, it attracted equity investment only through its R&D partnerships. The company also focused on revenue generation through licensing its proprietary technology. After its net income became positive and it resolved a patent dispute with another pharmaceutical company, it started to attract equity investments through private placements. As equity finance and licensing revenues became its sources of funds, the company remained financially prudent, keeping its R&D expenditures at less than 50 percent of its revenues since 2004. During this period, however, stock options became an important source of income, especially for executives.

As Myriad Genetics reaped revenues from its diagnostics products, it attracted both private and public equity finance. There have been high levels of entry and exit of major shareholders. With booms in the company's stock price in both the early and late 2000s, Myriad executives have been able to reap very large gains from exercising stock options. Since the spin-off of the therapeutics division of the company in June 2009, R&D expenditures have decreased substantially, and the company's stock price appears to have become highly sensitive to the expectations of sales results. Myriad Genetics' stock price showed little sensitivity for over a month after the potentially landmark ruling on March 30,

2010 that overturned Myriad's patent monopoly over the BRCA1 and BRCA2 genes. On May 5, 2010, however, its stock price dropped by over 23 percent, and on the following day by over five percent, reaching lows that had not be seen for over two years.

As a joint venture of two biotech companies, Galapagos was dependent on capital injections from and the technology licenses of its founder companies in early years of existence. Subsequently it raised venture capital followed by public equity in its IPO. After the IPO R&D partnerships and private placements were the major sources of funds. The company adopted a proactive strategy to boost revenues through the acquisition of several service companies. Today the company generates more revenue than it receives through financial markets, owing to its broad spectrum of partnership activities as well as continuing support from governmental and non-profit institutions for its cutting-edge research on novel therapies over a wide variety of research areas. Over the past five years, the company's employment levels have increased rapidly, while executives and other employees have begun to augment their incomes through the exercise of stock options.

There are some tentative lessons that we can draw from these case studies that can serve as hypotheses for further research:

- Equity investors view biopharmaceutical companies as sources of speculative gains. Especially after the IPO, there is a strong tendency toward value extraction even for companies that still require years to reap the fruits of their research.
- Different firms pursue different financial strategies in the face of varying alternative sources of finance.
- Access to government funding is critical for companies to develop their proprietary technology. This funding may take the form of research grants to founders through universities or direct grants to the company. In the case of Pharmacyclics, for example, both types of government support have been critical.
- The content of proprietary technology, therapeutic research area, and/or coverage of patents also has a major impact on the development of the company's financial strategy. This content is a determinant of forms of partnership, relations with competitors, and further acquisition of competencies (through in-licensing, cross-licensing, M&A, joint ventures), with the need for finance often driving the company's business strategy.
- Whatever a company's business and financial strategy, compensation through the exercise of stock options becomes important to executives and employees after the IPO, with short-term stock-price fluctuations providing them with windows of opportunity to reap the gains. This focus on the possibilities for short-term financial gain stands in stark contrast to the inevitably long-term and sustained investments that the companies must make to research and develop innovative products.

In our next stage of research, we intend to undertake:

- Comparative analyses of partnerships, focusing on the purpose and importance of alliances for the different partners;
- Detailed analyses of the ways in which short-term financial gains from stock-option exercises may conflict with the long-term financial requirements of product development;
- Detailed analyses of the importance of government funding for the drug development process, including not only the amount and forms of finance (research grants and financial subsidies) but also the extent and form of organizational integration of the publicly-funded knowledge-creation process with product development by the business enterprise;

- Detailed mapping of the various scientific and financial contributions to the development of biopharmaceutical products by parties such as scientists, research institutes, early investors, and founders of start-ups to determine the relation of these contributions to the ultimate sharing of the gains from innovative enterprise (the case of Myriad Genetics provides a prime case for such research);
- Methodological specification of how to collect information about the drug development process required for this type of research, how to compare and integrate qualitative and quantitative data derived from a variety of sources, and why it is critical to have a dynamic theory of innovative enterprise as an integrative analytical framework.

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