

Biotechnology financing dilemmas and the role of special purpose entities

Leora Schiff & Fiona Murray

Before they fell into disfavor, legally independent affiliates of biotech companies—special purpose entities—had supported the development of several blockbuster drugs. Are they about to stage a comeback?

Biotech firms attempting to make the transition from early-stage R&D to fully integrated companies with robust pipelines face a daunting financial challenge. Given that the extraordinary costs and time required to bring not one but a series of successful compounds to market cannot be sustained through operational revenues, firms are forced to use a range of external financing sources. Although public and private equity are among the largest and best known financing sources, a more esoteric financing vehicle, the special purpose entity (SPE), has played a significant role in the evolution and success of some of the most important biotech firms in the industry. Companies including Amgen (Woodland Hills, CA, USA), Genentech (S. San Francisco, CA, USA) and Genzyme (Cambridge, MA, USA) used SPEs in the 1980s and 1990s to fund critical R&D projects that resulted in the commercialization of highly successful drugs. But, in the mid-nineties, SPEs began to fall out of favor, and many members of today's biotech community are unfamiliar with both the nature and the historic role of these vehicles.

With the challenges of the current funding environment, interest in SPEs is rising once again among biotech's management and investment communities in the hopes of resurrecting these sophisticated financing vehi-

*Leora Schiff is currently an independent consultant working in Cambridge, Massachusetts, USA. She undertook the research that forms the basis of this article while an MBA student at MIT Sloan School of Management. Fiona Murray is on the Faculty at the MIT Sloan School of Management, 50 Memorial Drive E52-551, Cambridge, Massachusetts 02142, USA.
e-mail: leora.schiff@sloan.mit.edu*



Can investor expectations and the financing needs of companies be shuffled in the right way to make special purpose entities a winning combination?

cles. The proposal to reinvent SPEs is met with skepticism by some and enthusiasm by others but with little comprehensive data and analysis of their nature, use and role in the industry. To fill this gap, we undertook a detailed analysis of the history of SPEs to shed light on their characteristics, strengths and weaknesses. Our research includes a comprehensive listing of all known SPEs used by biotechnology companies, their sponsors and related R&D projects; in addition, we've interviewed leading industry experts.

Sustainability and external sources of capital

Historically, the biotech industry has relied

on three major sources of outside funding: the government, the capital markets (which include public and private equity, debt and SPEs) and corporate partners. Of these sources, the most important have been the equity markets and corporate partnerships. Between 1991 and 1998 the equity markets provided over \$34 billion to biotech companies, whereas corporate partnerships provided an additional \$20 billion¹. From July of 1998 to June of 2000, two years that straddled the biotech bubble, the amount of capital raised through private and public equity jumped to \$17.1 billion².

However, equity has serious drawbacks for companies trying to achieve sustainability. The cyclical nature of the equity markets has made access to capital as much an issue of timing as of pipeline success and one that can determine the very survival of a biotech company. Even under the best of circumstances, public and private equity capital has a high cost, because investors want significant returns to mitigate the risk of biotech investments. In a down market, the cost can be prohibitively high, assuming that it is available at all. Finally, each new round of equity dilutes the stake of the existing shareholders. Given the extraordinary amount of capital required to take a drug to market, it would be difficult if not impossible to fund the entire process uniquely with equity without destroying shareholder value³.

Corporate alliances, typically established between a biotech firm and large pharmaceutical partner, provide an important alternative source of capital, particularly in market down-cycles. Such alliances can cover the expenses of early-stage drug development through a combination of technology access fees, R&D costs (in terms of full-time equivalents) and milestones, as well as equity invest-

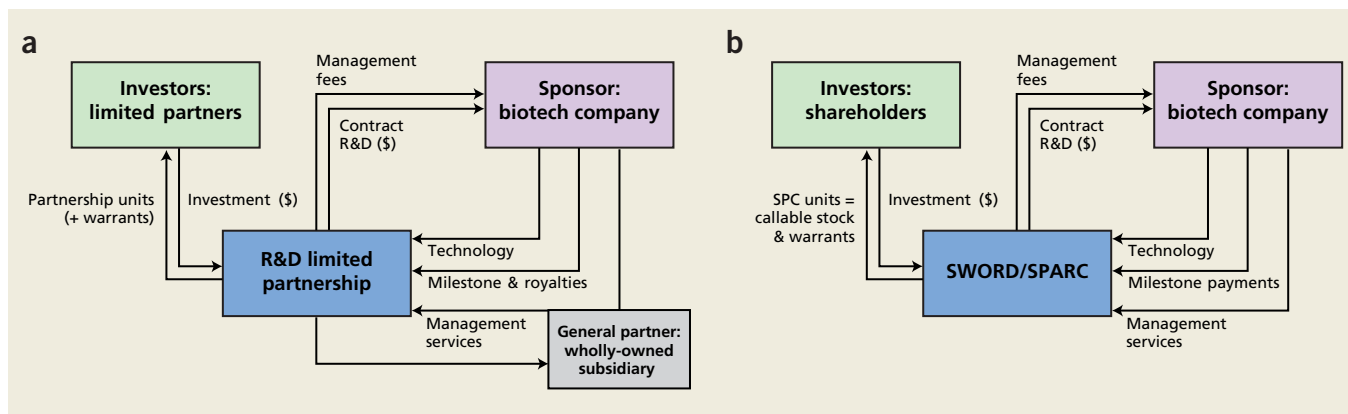


Figure 1 SPE structure. (a) Structure of R&D limited partnerships. (b) Structure of special purpose corporations.

ments that are often made at a premium. In addition, strategic alliances provide important external validation of the company and its technology, as well as access to the complementary assets of the partner.

Nonetheless, corporate partnerships have important limitations as a source of capital. First and foremost, the biotech company generally cedes the lion's share of the profits from any successful drugs issuing from the partnership to the larger partner⁴. In addition, the traditional division of labor in such relationships places upstream tasks in the drug development process in the hands of the biotech firm, and leaves the late-stage clinical trials and marketing to the pharmaceutical partner. This makes it difficult for smaller biotech companies to develop downstream assets and capabilities. Codevelopment and copromotion deals have shifted the balance more towards the middle, giving biotech

companies the opportunity to integrate farther down the value chain into later stage activities and to share more equally in the profits. However, the best they can hope for in such deals is a 50-50 split of the profits. Overall then, corporate partnerships have been an important means for biotech companies to get their drugs to market, but the terms of the partnerships have limited their ability to mass the physical assets, personnel, institutional knowledge and capital reserves necessary to push towards full integration and sustainability.

Special purpose entities

In 1982, early in the history of the biotech industry, in recognition of the limitations of the equity markets and the relatively limited interest in alliances on the part of pharmaceutical firms, industry pioneer Genentech, working with PaineWebber (now USB Fin-

ancial Services, New York), set about establishing alternative financing vehicles. Borrowing a vehicle widely used in the real estate and oil industries, they created the first biotech R&D limited partnership, Genentech Clinical Partners, to fund the development of recombinant human growth hormone. In so doing, they introduced an alternative source of external financing that helped to solve the dilemma of how biotech companies could reach sustainability: the SPE.

Structured around specific technology projects, SPEs were complicated financial vehicles that functioned as independent legal entities. These vehicles took one of two general forms: R&D limited partnerships (LPs) or special purpose corporations (SPCs) (Fig. 1). SPCs were more widely known by the brand names of SPARCs (special purpose accelerated research corporations) and SWORDS (stock and warrant off-balance-

Box 1 Glossary

Special purpose entity (SPE). A business entity formed solely to carry out specific and defined tasks, typically used for accounting purposes to separate the financial implications of distinctive activities. Used in the biotech industry for specific R&D projects.

Limited partnership (LP). An entity with one or more general partners who manage the business and assume legal debts and obligations, and one or more limited partners, who are liable only to the extent of their investments. Limited partners enjoy rights to the partnership's cash flow, but are not liable for company obligations.

R&D limited partnership (R&D LP). A form of SPE with a limited partnership structure formed by a biotech company to undertake a specific R&D project. The general partner is a wholly owned subsidiary of the biotech company and the limited partners are individual investors.

Special purpose accelerated research corporation (SPARC). Structured as special purpose corporations (SPCs) rather than as a limited partnership, the SPARC issues unit interests through public

offerings to institutional and individual investors. The corporation undertakes a defined research project, with contracts from the biotech firm to develop the research for the SPC. The key distinction from R&D LPs is corporate oversight, which includes individuals from outside the biotechnology firm. Typical investors also differ being large institutions rather than individuals.

Stock and warrant off-balance-sheet R&D corporation (SWORD). These are the same as SPARCs—the alternative name being coined by different investment banks. Each unit has one share of the venture's common stock that can be called by the sponsoring parent and one warrant to purchase a share of the common stock of the parent that permits the investor to maintain a position in the results of the venture.

Off balance sheet. This element of SWORDS and SPARCs means that the financial statements of the separate organization are designed to have no impact on the sponsoring 'parent,' and the financing comes from a public offering of units in the R&D venture.

sheet R&D corporations) (see **Box 1** for a glossary).

R&D LPs and SPCs both provided biotech companies with the means of transferring the rights to specific R&D projects to a group of outside investors. The outside investors would purchase interests in the SPE, interests that often included warrants on the sponsoring biotech company's stock (giving the investor the right to buy the stock at some later date). The SPE would then use these funds to in-license the defined technology or compound from the sponsoring biotech company and to contract that company to perform the R&D for the project. After a few years, the biotech company would have the right to exercise an option to buy back the project from the SPE.

The relationship between the investors, the sponsoring biotech company and the SPE was governed by a series of legal agreements that defined the purpose of the SPE. This included the nature of the technology to be developed, the management of the SPE (for R&D LPs, generally executives from the biotech company and for SPCs, an independent board of directors with a minority of biotech firm executives), the terms and obligations of the R&D contract with the sponsoring biotech firm and the terms of the purchase option between the biotech sponsor and the investors. SPEs offered important incentives both to the biotech sponsors and to the investors. For the investors, the fundamental

incentive was a significantly higher return than that offered by equity investments.

Although broadly similar in concept and structure, the target pool of investors and the specific deal components that collectively provided these high returns to investors differed between the R&D LPs and the SPCs.

In R&D LPs, the target investors were wealthy individuals, many of whom were eager to invest in the exciting new field of biotech. Through 1985, a big attraction for these investors was the tax benefit from pass-through losses from the R&D LPs, a benefit that disappeared with the Tax Reform Act of 1986. Following the change in the tax code, other deal components, such as product royalties and warrants on the sponsoring companies' shares, were factored in more heavily to provide an attractive return. For the SPCs, the target was large institutional investors. These investors were attracted not only by the high returns offered by the buyback terms for the shares in the SPC and potential return on the warrants on the sponsor's stock, but also by the higher liquidity of the SPCs over the R&D LPs—arising because unit interests in SPCs were registered on exchanges such as AMEX and NASDAQ and could be traded freely.

Advantages of SPEs

For the sponsoring biotech company, SPEs had several important advantages over other sources of financing. Through SPEs, companies were able to diversify the risk of their

early-stage R&D by transferring projects to outside investors with the option to buy back the rights to the projects at a later date.

SPEs thus enabled companies to invest in projects that they could not otherwise afford or to accelerate promising projects with the increased capital available through an SPE. In addition, the SPEs had a profit and loss (P&L)-sparing effect that was beneficial to those companies nearing or at profitability; the sponsoring company was able to book contract revenues that offset the R&D expense associated with an SPE-funded project. Moreover, when the biotech sponsor bought back the rights to the project, it was booked as in-process R&D, an extraordinary event that was generally not factored into the company's earnings growth trends by the market analysts and therefore provided an additional boost to earnings trends. Finally, the companies gave up a much smaller portion of the profits from successful drugs to the SPE investors than they would have had they funded their R&D through a corporate alliance, and they were able to invest in the development of the downstream capabilities necessary for achieving full integration. SPEs therefore enabled the sponsoring biotech companies to engage in early-stage R&D projects while they continued to support the development of late-stage projects (that is, they could develop their drug pipelines while concurrently moving down the value chain).

Box 2 Enron—how not to run an SPE

As a result of the Enron (Houston, TX, USA) accounting scandal, SPEs have become associated with financial malfeasance and are viewed with suspicion. However, they have important, legitimate roles in current business practice. FASB continues to support the validity of SPEs in "isolating assets or activities to protect the interests of creditors or other investors or to allocate risks among participants"⁵.

Although special purpose entities can provide legitimate benefits for investors, this did not occur in the case of Enron. Among the irregularities in the Enron SPEs, two are of particular note: first, Enron provided all of the funds that were invested in certain SPEs that it sponsored but failed to consolidate the SPEs' assets and liabilities onto its own financial statements, ignoring the requirement of Generally Accepted Accounting Practices (GAAP) of a minimum of 3% funding from independent investors; and second, Enron provided the capital for its SPEs in the form of Enron shares, and then improperly accounted for fluctuations in the price of the Enron stock owned by the SPEs (this resulted in an overstatement of income and an understatement of losses from its equity investments)⁵. The complexity of Enron's financial engineering enabled Enron executives to obfuscate the actual liability that these SPEs represented to the parent company, surprising investors when

Enron's financial house of cards finally collapsed.

By contrast, the special purpose entities used by biotech companies have involved legitimate funding from outside investors. Accounting treatment of these financial vehicles by the biotech sponsors has been in accordance with prevailing accounting standards, with detailed information regarding the SPEs being provided in the Management's Discussion & Analysis section of these companies' annual reports. With FASB's most recent change to the rules governing the consolidation of SPEs, biotech sponsors have already begun consolidating active SPEs onto their financial statements. Where these vehicles may raise concerns on the part of investors is in the realm of governance; an R&D LP is governed by a wholly owned subsidiary of the biotech sponsor acting as general partner, whereas in the case of the SPCs, executives of the biotech sponsor act as directors, giving the sponsor minority representation on the board of directors. Because of the involvement of the biotech sponsor in the decision-making process of the SPE, extreme care is required to ensure the protection of both the SPE's and the sponsor's investors. To date, the investors of two SPEs, Tocar II and Synergen Clinical Partners, have mounted class action suits against the SPEs and sponsoring biotech companies, charging conflicts of interest; both were settled out of court.

SPE use in the biotech industry

From the introduction of the R&D LP by Genentech in 1982 to the creation of the SPC in 1989, SPEs gained increasing popularity as a means of financing R&D projects. These financing vehicles had two key characteristics that made them particularly suited for more mature biotech firms. First, the SPE sponsors were generally publicly traded companies because the repurchase of the rights to the R&D project by the sponsor was most often in the form of an exchange offer. SPE units often included warrants on the sponsor's common stock; thus, investors needed to be confident that the sponsoring company's stock would appreciate during the life of the SPE. Second, the project transferred to the SPE needed to be well defined and attractive to investors looking for high-risk/high-return invest-

ments. It was also critical that the project could be sufficiently matured during the life of the SPE so that the project's risk was substantially reduced, thus justifying the relatively high cost of repurchase by the sponsoring company. This bias is reflected in the list of SPEs that we have identified through archival research and interviews with leading industry experts (see Table 1).

Starting in 1982, we found evidence for 39 SPEs raising a total of more than \$1.4 billion up until 2001, of which the largest single SPE was Dura Pharmaceutical's Spiros Development Corporation II SPC, which raised \$94 million in 1997 for a suite of applications of the Spiros technology, although \$75 million was a 'parent contribution' that came from Dura itself. (Dura was founded in 1983 and acquired by Elan Pharmaceuticals, Dublin, in

2000.) The largest fund raised by an SPE uniquely from outside investors was Centocor's (Malvern, PA, USA) SPC, Tocor II, which raised \$90 million in 1992. Three biotechnology companies made the most significant use of SPEs: Genentech with four R&D LPs raising over \$195 million; Genzyme, which created two SPCs and two R&D LPs that raised a total of \$179 million; and Centocor, which raised a combined total of \$257 million through six different SPEs between 1984 and 1992. With each successive market cycle, more money was raised through SPE offerings, reaching a peak in 1992 (Fig. 2).

Despite their obvious appeal to biotech sponsors, SPEs fell precipitously out of favor with investors in 1993, with only five financed after that. What change caused investors to turn away from SPEs? To understand this market shift, it is necessary to understand the expectations of the investors and the biotech sponsors involved in the formation of SPEs. Ostensibly, investors could expect high returns in exchange for assuming the relatively high risk associated with early-stage R&D projects. However, the reality was somewhat different. Between the investors and biotech sponsors, industry commentators have suggested that there existed a tacit understanding that the biotech companies would buy back the rights to the R&D projects, irrespective of the projects' success or failure. The rationale was that the sponsors would need to ensure the satisfaction of the SPE's investors if they intended to sponsor future SPEs. Fortunately for the sponsoring companies, the earliest R&D LPs were wildly successful, encouraging more investors to enter the SPE market. Of the drugs developed with the support of SPE funds, several are among the most important drugs developed by the biotech industry. These are: tissue plasminogen activator (Activase; Genentech); human growth hormone (Protropin/Neotropin; Genentech); granulocyte colony stimulating factor (Neupogen; Amgen); glucocerebrosidase (Ceredase/Cerezyme; Genzyme) and tumor necrosis factor receptor (p75)-Fc fragment fusion protein (Enbrel; Immunex (now Amgen), Seattle, WA, USA).

Starting in 1989, however, several biotech sponsors renegotiated the terms of their purchase option agreements, either because of the limited success of the SPEs' projects or because of the sponsors' inability to pay the purchase price originally negotiated. Among the most visible of these renegotiated deals was that of Tocor II with Centocor, which resulted in a 1993 class action suit by the investors that was later settled out of court. With this 'wake-up call' investors realized that

Table 1 Listing of all known SPEs

SPE	Sponsoring company	Nature of SPE	Offer year	SPE money raised (\$ millions)
Genentech Clinical Partners, LP	Genentech	R&D LP	1982	\$55.6
R&D LP	Scios (Cal. Biotech)	R&D LP	1982	\$27.5
Cetus Healthcare, LP	Cetus	R&D LP	1983	\$75.0
Genentech Clinical Partners II, LP	Genentech	R&D LP	1983	\$34.0
Biogen Medical Products, LP	Biogen	R&D LP	1984	\$30.0
Centocor Oncogene Research Partners, LP	Centocor	R&D LP	1984	\$5.0
Centocor Cardiovascular Imaging Partners, LP	Centocor	R&D LP	1985	\$23.2
Genentech Clinical Partners III, LP	Genentech	R&D LP	1985	\$33.2
Centocor Partners II, LP	Centocor	R&D LP	1986	\$54.3
Cetus Healthcare, LP II	Cetus	R&D LP	1986	\$62.0
Chiron Ophthalmic Research Partners	Chiron	R&D LP	1986	NA
Amgen Clinical Partners, LP	Amgen	R&D LP	1987	\$83.6
Centocor Partners III, LP	Centocor	R&D LP	1987	\$52.8
Genzyme Clinical Partners, LP	Genzyme	R&D LP	1987	\$10.0
Tocor	Centocor	SPC	1989	\$31.0
Genentech Clinical Partners IV, LP	Genentech	R&D LP	1989	\$72.5
Genzyme Development Partners, LP	Genzyme	R&D LP	1989	\$36.7
Receptech	Immunex	SPC	1989	\$27.0
Neozyme	Genzyme	SPC	1990	\$47.3
SciGenics	Genetics Institute	SPC	1991	\$42.0
Aramed	Sicor (Gensia)	SPC	1991	\$53.0
Gensia Clinical Partners	Sicor (Gensia)	R&D LP	1991	\$26.3
Alkermes Clinical Partners, LP	Alkermes	R&D LP	1992	\$46.0
Tocor II	Centocor	SPC	1992	\$90.0
Cephalon Clinical Partners, LP	Cephalon	R&D LP	1992	\$40.0
CytoRad	Cytogen	SPC	1992	\$35.0
Neozyme II	Genzyme	SPC	1992	\$85.0
Dura Delivery Systems, Inc.	Dura Pharm.	SPC	1993	\$13.0
Spiros Development Corp.	Dura Pharm.	SPC	1995	\$28.0
ALRT (Allergan Ligand Retinoid Therapeutics)	Ligand (Allergan)	SPC	1995	\$33.0
Spiros Development Corp. II	Dura Pharm.	SPC	1997	\$94.0
ICOS Clinical Partners, LP	ICOS	R&D LP	1997	\$79.8
	Total	32		\$1,426
	Average			\$46.0
	Standard deviation			\$24.2

© 2004 Nature Publishing Group http://www.nature.com/naturebiotechnology

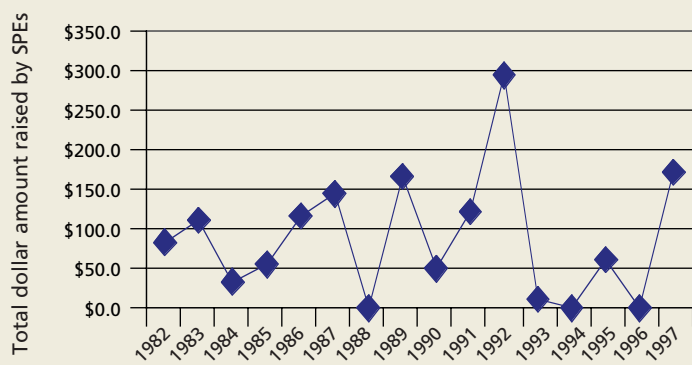


Figure 2 Capital raised through SPEs from 1982–1997.

these were in fact risky investments, and their interest in these vehicles cooled significantly. At around the same time, the market for secondary equity offerings and private investments in public equity opened up considerably starting in 1995, providing biotech companies with access to large amounts of less expensive capital. In addition, in the latter half of the 1990s, pharmaceutical companies became much more generous in the terms of their partnering agreements as they felt increasing pressure on their pipelines. Overall, SPEs fell into disfavor with investors and biotech companies alike.

The Impact of SPEs

Although they have fallen into disuse, SPEs have played an important role in the development of the biotech industry. Yet the impact of these financing vehicles on the long-term success of the sponsoring biotech companies has yet to be assessed. The deals that were formed were very visible because they involved for the most part the leading biotech companies of the day. Because these companies were already perceived as being industry leaders, what role did SPEs play in their overall success? Given the significant hurdles to sponsoring SPEs, few companies were in a

position to be sponsors and relatively few SPEs were formed. Those that had access to this source of financing and did create SPEs were by necessity among the more successful and sophisticated companies. Thus, although the correlation between SPEs and success is relatively obvious, the question of causality—did SPEs indeed contribute to the success of such firms—is difficult to establish.

As a means of approaching this issue, we did several analyses. First, we examined the relative capital contribution of SPEs compared with initial public offerings (IPOs) for those firms that used SPEs. Second, we examined the success of SPEs in the creation of successfully marketed drugs. Finally, we compared the use of SPEs among different cohorts of biotech firms. For the purpose of this study, the subject group was limited to those biotech companies engaged in the development of biopharmaceutical products that had ever crossed the threshold of \$1 billion in market capitalization.

Fund raising. The 19 companies using SPEs in the subject group sponsored a total of 21 R&D LPs and 15 SPCs. Financial information was available for 16 of these companies. Through the initial SPE offerings, these companies were able to raise over \$1.4 billion; the amount raised through these offerings was on average 1.5 times the amount of money that these companies raised through their IPOs. If

Table 2 Funds raised through SPEs versus equity (\$ millions)

Company	Private noncorporate equity: pre-IPO	Corporate equity: pre-IPO	Public equity	Private equity: post-IPO	Corporate equity: post-IPO, preacquisition	SPEs	Tracking equity stock	Company total
Alkermes	11.19	0	60.37	389	35	69.77		565.33
Amgen	18.8	0	200.1	0	5	104.8		328.7
Biogen	0.49	47.9	243.73	101.6	0	40.9		434.62
Cephalon	9.91	5	215.78	831.83	40.8	40		1143.32
Centocor	7.3	0	243.03	113.37	97	256.2		716.9
Cetus	5	7	212.092	3	14.25	137		378.342
Cytogen	3.08	22.45	121.65	136.32	3	35		321.5
Dura Pharmaceuticals	32.58	13.88	435.43	298.55	4.25	135		919.69
Genentech	1.475	10.425	89.5	5.1	80	195.3		381.8
Genetics Institute	25.6	24.21	204.03	0	0	42		295.84
Genzyme	9	0	349.87	271.2	0	179	79.7	888.77
ICOS	33	0	620.61	23.29	0	128.56		805.46
Immunex	4	0	225.35	0	20	27		276.35
Ligand Pharmaceuticals	12	30	85.34	47.5	206.9	45.5		427.24
Scios	5.4	0	186.05	120.75	32	27.5		371.7
Sicor/Gensia	26.34	15	349.2	209.4	0	79.3		679.24
Total	205.2	175.9	3,842.1	2,550.9	538.2	1,542.8	79.7	8,934.8
Average	12.8	11.0	240.1	159.4	33.6	96.4	79.7	558.4

Owing to a lack of data regarding Chiron Ophthalmic Research Partners, Chiron was not included in this table. Corporate equity is equity positions taken by corporate partners. Post IPO refers to secondary and follow-on equity offerings. Preacquisition refers to the company before any acquisition activity. Tracking stock equity refers to public offerings of tracking stocks. SPE totals include warrants exercised by SPE investors where such warrants are specified in the companies' annual reports. Given that not all warrant exercises could be documented, the SPE values are an underestimate of the true amount of money raised. The \$50 million raised by Cephalon through Anthem was not included as this SPC was unwound only months after its public offering.

the money raised through the exercise of warrants on the sponsor's stock is included, 16 of these SPE-users raised over \$1.5 billion through SPEs for an average of \$96.4 million per company; however, SPEs were highly variable in size, increasing over the period from their first introduction in 1982 to \$94 million in 1997 with Dura Pharmaceutical's Spiros Development Corporation II.

As a fraction to the total amount of funding raised, SPEs amounted to 18.5% (where the total includes private equity, public equity, and corporate equity both before and after the IPO, in addition to SPE funds), although the funds raised from SPEs exceeded the actual IPO amount for 11 of the 16 companies (Table 2).

Product development. Projects that biotech companies funded through SPEs ranged from enzyme and hormone replacement therapies to antibody therapies and drug delivery technologies. Of the 36 SPEs sponsored by companies in the study group, 14 resulted in the development of products that have reached the market. In addition, Scios (Fremont, CA, USA) acquired a company with an active SPE—Synergen Clinical Partners and Nova Technology Limited Partners—that resulted in additional marketed products. Three SPEs—Genentech Clinical Partners, Genzyme Development Partners and Neozyme—each resulted in more than one commercial product. In all, 15 drugs and four diagnostic tests, whose development was supported in part by SPEs, have reached the market (Table 3). Eight of the 36 SPEs have had all of their projects terminated.

It is unclear which of the projects associated with the remaining 14 SPEs are still under development.

The most notable successes include: Neupogen, which is responsible for over \$10 billion in revenues for Amgen; Genentech's portfolio of SPE-funded products, which has generated a total of \$6.6 billion; Genzyme's portfolio of SPE-funded products, which has generated a total of \$3.4 billion; and Enbrel, which earned \$1.8 billion for Immunex before its acquisition by Amgen. Collectively, the SPE-funded drugs and diagnostic tests that have reached the market have generated approximately \$23 billion in revenues to date. In the case of Genzyme and the development of Ceredase, it is quite possible that funding through an R&D LP was the only option given that Genzyme had just made its IPO the year before, making it too soon to raise additional equity, and pharmaceutical partners would not be interested in investing in the development of an orphan drug with what was then thought to be an extremely limited upside.

Relative success. Examining the 21 firms that engaged in SPEs, we find that 19 crossed the threshold of \$1 billion in market capitalization. Furthermore, these companies have had a significant impact on the entire biotech sector over the past 20 years, having developed many of the industry's flagship products, providing evidence of the potential of biotech firms as sustainable entities. To examine their contribution, we compiled a comprehensive list of 102 biotech companies, engaged in the development of biopharma-

ceuticals, that had crossed the market capitalization threshold of \$1 billion. SPE-users were disproportionately represented in the top ten biotech firms by market capitalization, particularly in the early days of the industry, and this trend has continued over most of the past two decades.

Table 4 shows the number of companies with a market capitalization of \$1 billion or greater and the number of those companies that used SPEs. From 1985–1994, the proportion of companies in the top tier of the biotech industry using SPEs was 100%. With the exception of the boom years of 1999–2001, that proportion has remained in excess of 45%. Amgen, Genentech, Genzyme, Chiron (Emeryville, CA, USA) and Biogen (Cambridge, MA, USA) have remained in the industry's top tier continuously anywhere from 13 to 19 years since first crossing the \$1 billion threshold. In all, six of the current top ten biotech companies ranked by market capitalization have used SPEs for R&D financing.

Several companies that used SPEs have yet to reach profitability—Alkermes (Cambridge, MA, USA), Cytogen (Princeton, NJ, USA), ICOS (Dublin), Ligand Pharmaceuticals (San Diego, CA, USA) and Scios. Others were acquired and no longer exist as independent business entities—Centocor, Cetus, Dura Pharmaceuticals, Genetics Institute, Immunex and Synergen. However, at least some of these companies chose the path of acquisition for reasons other than an inability to survive as independent organizations. Although it has also been acquired (by Hoffmann-La Roche, Nutley, NJ, USA),

Table 3 Marketed products generated by SPEs

SPE	Sponsoring company	Marketed product
ALRT (Allergan Ligand Retinoid Therapeutics)	Ligand/ Allergan joint sponsorship	Panretin (alitretinoin)
Amgen Clinical Partners, LP	Amgen	Neupogen
Centocor Cardiovascular Imaging Partners, LP	Centocor	Myoscint (imciromab pentetate)
Centocor Partners III, LP	Centocor	CentoRx (Centocor)/ Reopro (Lilly) (Abciximab)
Ceredase Partnership	Genzyme	Ceredase
CytoRad	Cytogen	ProstaScint (capromab pendetide)
Genentech Clinical Partners II, LP	Genentech	Activase, TNKase, Cathflo Activase
Genentech Clinical Partners, LP	Genentech	Protropin, Nutropin & Nutropin AQ
Genentech Clinical Partners, LP	Genentech	Actimmune (Intermune) (interferon γ -1b)
Genzyme Development Partners, LP	Genzyme	Septrafilm (hyaluronic acid membrane)
Genzyme Development Partners, LP	Genzyme	Sepramesh (polypropylene mesh)
Genzyme Development Partners, LP	Genzyme	Sepragel (hylan B gel)
Neozyme	Genzyme	Thyrogen (thyrotropin α)
Neozyme	Genzyme	Cholesterol tests
Neozyme	Genzyme	Synthetic phospholipids
Nova Technology Limited Partnership	Nova Pharmaceutical/Scios	Gliadel (wafer with carmustine)
Receptech	Immunex	Enbrel
Synergen Clinical Partners, LP	Amgen/Synergen	Kineret (interleukin-1 receptor agonist)

Genentech is still traded independently on the public markets.

Of the companies analyzed, ten biopharmaceutical companies were identified as being mature, sustainable firms. These firms are Amgen, Genentech, Genzyme, Chiron, Biogen, Cephalon (West Chester, PA, USA), SICOR (Irvine, CA, USA), MedImmune (Gaithersburg, MD, USA), IDEC and IDEXX Laboratories (Westbrook, ME, USA). (This analysis was done before the announcement of the Biogen-IDEC merger; at the time, both Biogen and IDEC Pharmaceuticals satisfied the criteria used in defining sustainable biopharmaceutical companies.) The criteria used in this assessment were that these companies were profitable, had a market capitalization in excess of \$1 billion and had credible pipelines. Of the ten companies listed, seven used SPEs to fund R&D projects; of these, three companies sponsored SPEs resulting in extremely successful commercial products.

Relic or resurrection?

It is clear that a strong association exists between the leading companies in the biotech industry and SPE use. However, it is far more difficult to assign causality in this relationship. Although companies that use SPEs have dominated the industry for almost two decades, these companies had already attained a certain level of maturity in order to access these financial vehicles. On the other hand, these firms were far from being sustainable companies at the time of their first SPEs. In addition, SPEs funded many of these companies' most important R&D projects, enabling a number of significant commercial successes that resulted in sizable revenue streams for the sponsoring companies. If these companies were already on the road to success, then it appears that SPEs helped them reach their goal of sustainability much faster than they would have otherwise. Furthermore, one cannot dispute the fact that for a biotech company, access to additional capital is critical. SPE funding enabled companies to invest in additional early-stage R&D projects, increase their technical staff, add to their institutional knowledge and develop additional pipeline assets, all of which added considerable value. For those projects resulting in successful products, the sponsoring companies were able to

Table 4 SPE users in biotech's billion-dollar firms

Year	Number of billion-dollar biotech firms using SPEs	Total number billion-dollar biotech firms	Biotech firms using SPEs (%)
1985	1	1	100.0
1986	2	2	100.0
1987	1	1	100.0
1988	1	1	100.0
1989	2	2	100.0
1990	2	2	100.0
1991	6	6	100.0
1992	9	9	100.0
1993	7	7	100.0
1994	7	7	100.0
1995	7	8	87.5
1996	8	10	80.0
1997	8	17	47.1
1998	9	20	45.0
1999	8	28	28.6
2000	13	90	14.4
2001	12	52	23.1
2002	12	32	37.5
Total	19	102	18.6

hold onto the vast majority of the resulting revenues; these revenues were not only a source of cash that could be used to fund future growth, but also a source of positive earnings that enabled the companies' stock prices to appreciate considerably. For those fortunate companies that had assembled the necessary technical and managerial ingredients for success and that were able to bring their projects to fruition, SPEs helped propel them into the forefront of the biotech industry.

With their undeniably important role in the annals of biotech financing, the question remains as to whether SPEs will become an interesting relic of financing lore or reemerge, perhaps restructured, to enable a new generation of products to be developed. On the one hand, the aftermath of SPE-related litigation and the accounting scandals of 2001 have pushed investors toward increased simplicity and transparency in their investments (Box 2). In addition, new standards on the consolidation of financial vehicles issued by the US Financial Accounting Standards Board (FASB; Norwalk, CT, USA) in early 2003 have eliminated the P&L-sparing of tradi-

tional SPEs. On the other hand, tough financial markets, the increasing cost of drug development and a growing reluctance on the part of big pharma to recreate the mega-deals of the past make the search for alternative funding vehicles more crucial than ever.

For SPEs to make a comeback, though, they will need to be restructured to address the needs of both the investors and the biotech sponsors in this changed market environment. However, given the ability of these vehicles to accelerate company growth, it is not surprising that according to our interviews and informal discussions with executives and bankers, some investment banks are attempting to restructure SPEs to make them attractive both to biotech companies and high-risk investors under current market conditions. As the biotech and investment communities work to redefine the structure of SPEs to make them mutually attractive, they will need to address such issues as the changes in the rules for consolidation and investors' expectations of greater transparency in governance practices. One possible direction that the SPEs might take is to become entities with real substance that have decision-making control. Such an entity would not need to be consolidated onto the sponsoring company's financial statements, preserving the P&L-sparing benefits of the original SPEs; however, the loss of control by the sponsor might make such vehicles significantly less attractive.

ACKNOWLEDGMENTS

The authors would like to thank the two dozen executives, investment bankers, investors and accountants who generously gave their time and shared their opinions in the interviews that form the basis for much of this research.

1. Recombinant Capital. Year-end '98 financing numbers: A Tale of Two Biotech. *Signals Magazine*, (<http://www.signalsmagazine.com>) February 7, 1999.
2. Ernst & Young LLP. Convergence: Ernst and Young's Biotechnology Industry Report, Millennium Edition (Ernst & Young, New York, 2000).
3. Solt, M.E. SWORD financing of innovation in the biotechnology industry. *Financial Management* **22**, 173-187 (1993).
4. Edwards, M. *et al.* Value creation and sharing among universities, biotechnology and pharma. *Nat. Biotechnol.* **21**, 618-624 (2003).
5. Financial Accounting Standards Board. Exposure Draft, Proposed Interpretation: Consolidation of Certain Special Purpose Entities, an interpretation of ARB NO. 51, File ref. no. 1082-200 (FASB, Norwalk, CT, June 28, 2002).