Business History
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713634500

Collaboration - a competitor's tool: The story of Centocor, an entrepreneurial biotechnology company

Lara Vivienne Marks [ab]
[a] Cambridge University, Cambridge, UK [b] Open University, Buckinghamshire, UK

Online Publication Date: 01 July 2009

To cite this Article Marks, Lara Vivienne(2009)'Collaboration - a competitor's tool: The story of Centocor, an entrepreneurial biotechnology company',Business History,51:4,529 — 546
To link to this Article: DOI: 10.1080/00076790902998512
URL: http://dx.doi.org/10.1080/00076790902998512

Business History
Vol. 51, No. 4, July 2009, 529–546

Routledge
Taylor & Francis Group

Collaboration – a competitor's tool: The story of Centocor, an entrepreneurial biotechnology company

Lara Vivienne Marks*

Cambridge University, Cambridge, UK and Open University, Buckinghamshire, UK

Biotechnology companies have relied on alliances for survival and growth since their inception. This history of Centocor illustrates the pivotal role collaborations played for pioneers in the industry. Five years after its founding Centocor had become a competitive and profitable diagnostics company based on partnerships with research institutes and larger health care companies. In 1992, however, Centocor faced collapse, brought on by a departure from collaboration and going it alone in the development and marketing of the company's first therapeutic. What saved the company and enabled it to prosper in therapeutics was a reversion to the old strategy of collaboration.

Keywords: alliances; biotechnology; technology transfer; pharmaceutical; diagnostics

Introduction

Since their inception in the 1970s biotechnology companies have relied on alliances for their survival and growth. Based on company papers and interviews with key executives this history of Centocor illustrates the pivotal role collaborations played for pioneers in the industry and the factors decisive for successful collaboration.[1] Founded in 1979, three years after Genentech, the world's first dedicated biotechnology company, Centocor was among the first handful of biotechnology companies started in the 1970s.[2] By 1984 Centocor had become a highly competitive and profitable diagnostics company based on monoclonal antibodies (mabs). Much of its early success was built on partnerships with research institutes and larger health care companies. Through skilful networking Centocor's executives secured the scientific and technological expertise, products, capital and market distribution necessary to mature from a small start-up company to a significant player in the global diagnostic market. In 1992, however, Centocor faced imminent collapse, due in part to its executives' determination to go it alone in the development and marketing of the company's first therapeutic. What saved the company from extinction and allowed it to then prosper in therapeutics was a reversion to the old collaborative strategy.

*Email: lm272@cam.ac.uk

ISSN 0007-6791 print/ISSN 1743-7938 online

DOI: 10.1080/00076790902998512
http://www.informaworld.com

A pioneering company is born

In May 1979, Hilary Koprowski, a Polish virologist, immunologist and director of the Wistar Institute[3] partnered with Michael Wall, a MIT-educated electrical engineer and founder of several electronics, computer and biological start-up companies,[4] to start a new biotechnology company. Calling the company Centocor, Koprowski and Wall aimed to create, develop and market diagnostics and therapeutics based on mab technology, a technique that cloned specific antibodies (proteins produced by the immune system designed to attach to and inactivate foreign particles, or antigens) from a single cell. Mab technology was an unusual choice because most biotechnology companies in these years were investing in recombinant DNA technology, the genetic process of combining one piece of DNA with another.

Mabs were new to the scientific and commercial world. Since the late nineteenth century scientists had been searching for a way to develop medicines based on antibodies. They were handicapped, however, by the fact that for much of the twentieth century the methods for isolating and purifying antibodies were crude, making their supply uncertain and prohibitively expensive. In addition their key mechanism of binding to particular antigens was poorly understood, making them poor medical tools.[5] In 1975, however, there was a breakthrough when a post-doctoral student, George Kohler, and his mentor, Cesar Milstein, at the Laboratory of Molecular Biology, Cambridge University, devised a technique for the selection and reproduction of monoclonal (single) antibodies for the first time.[6]

Kohler and Milstein's method was quickly adopted by various academic and commercial laboratories globally, including Centocor's co-founder, Koprowski, and his Wistar team. Using cells donated by Kohler and Milstein, Koprowski and his colleagues began to develop mabs against the influenza virus and malignant cancer tumours.[7] Funded by government grants, this research formed the basis for patent applications in 1978. Granted in 1979 and 1980, these patents were the first mab patents and became Centocor's first technological platform for product development.[8]

Setting up office in downtown Philadelphia in May 1979, Wall, as the company chairman, started to build Centocor's executive with scientific support from Koprowski and the Wistar Institute. In August 1979 Wall recruited Hubert Schoemaker, a Dutch immigrant biochemist with a doctorate from MIT who had pioneered and built a highly successful diagnostics section at Corning Medical, a division of Corning Glass Works. Initially Centocor's vice president of operations and treasurer, Schoemaker soon became chief executive officer. Vincent Zurawski, a post-doctoral research associate from Harvard Medical School and Massachusetts General Hospital (MGH) who had worked on production methods for mabs also joined the team as chief scientific officer.[9]

The collaborative journey begins

Initially the founders decided to focus resources on diagnostics, predicting US$17 million in revenues by 1984,[10] with therapeutics as their long-term goal. Diagnostics were easier to develop and could win regulatory approval more easily than therapeutics, thereby enabling faster revenue growth.[11] In addition to developing diagnostic products they aimed to supply antibodies on contract to other companies for use in their proprietary diagnostic kits.[12]

Entering the diagnostics sector was ambitious. The US$2 billion diagnostics market was highly competitive, dominated at that time by health care giants like Abbott Laboratories, F. Hoffman-La Roche and Warner Lambert which had developed tests that could only be analysed through their own proprietary instruments. In 1979 two companies were already offering mabs on a commercial basis: Hybritech, a San Diego start-up founded in 1978 by Ivor Royston, a professor at the University of California San Diego and his research assistant Howard Birndorf, developing a mab-based hepatitis diagnostic; and Sera Lab, a British company (with which Cesar Milstein was involved) marketing several mabs to researchers.[13] The competitive landscape, however, quickly changed. By 1983 over 150 companies, including large pharmaceutical companies, had mab-based diagnostic programmes, and 23 such diagnostics were being marketed and another 100 were in the pipeline.[14]

From the start Wall and Koprowski saw collaboration as key to their business model. The very name 'Centocor' was derived from the words (1) 'cento' which describes (in Latin) an old garment made of hundreds of patches of material or a literary or musical composition made up of parts of other works; and (2) 'cor(e)' as in the centre.[15] Centocor's collaborative philosophy was unusual for the time. In 1979 most start-up biotechnology companies were trying to do everything internally from the discovery process through to development. Centocor's founders believed, however, that rather than depending solely on in-house research they should use internal skills to identify and fund prominent external researchers and laboratories working in areas the company wanted to develop and where appropriate license the technology.[16]

Central to Centocor's policy of collaboration was Wall and Schoemaker's remarkable ability to network.[17] By being well connected and plugged into the academic world, Wall and Schoemaker realised they stood a better chance of finding promising products at a relatively early stage when they were not unduly expensive.[18] As Schoemaker later put it 'We realized it was a lot cheaper to roam academe and pay a royalty back for what we developed than start our own research facilities. Collaboration was the best way to be competitive'.[19]

One of Centocor's strongest academic collaborations was with the Wistar Institute, fuelled in part by Koprowski's connection with the company. In 1979 Centocor signed three licensing deals with the Institute for rights to four approved and pending patents for diagnostic and therapeutic purposes. Centocor paid US$25,000 upfront and agreed to make royalty payments of 4–6% for any resulting products.[20]

Centocor's alliance with the Wistar was helped by the fact that the latter had its own charter and board. This allowed greater flexibility for academic–company collaboration than otherwise was normally possible in the late 1970s. Although the pioneering academic–company relationship between Centocor and the Wistar raised some concern about conflict of interest for one Wistar board member this was soon overcome.[21] The relationship set an important precedent for the partnerships Centocor entered thereafter.[22]

Centocor, like other biotechnology companies, was helped enormously by the passing in late 1980 of the Bayh-Dole Act, which established for the first time uniform guidelines for the patenting and commercialisation of government-funded academic research.[23] Between 1985 and 1990 Centocor's partnerships with research institutions grew from 15 to over 80 worldwide, many involving licence and option licence agreements.[24] These collaborations were vital to Centocor's business, providing materials for some of its early products.[25] Crucially, it allowed the

company to keep its costs to a minimum while increasing sales: between 1984 and 1990 Centocor's research and development (R&D) budget remained at the same level while its sales increased fivefold (see Figure 1).[26]

In addition to partnering with research institutions to fill its product pipeline, Centocor pursued marketing alliances. Facing a highly competitive environment, Wall and Schoemaker realised they could strengthen the company's market position by licensing agreements with companies that had well-established market positions and distribution channels. This would eliminate the time and expense of establishing Centocor's own distribution mechanism and facilitate faster entry to the market.[27] By 1983 61% of Centocor's product sales were made by major distributors. Two years later this had increased to 74%.[28]

Centocor's team deliberately secured agreements with key diagnostic companies whereby the companies would buy and sell Centocor's antibodies in completed test kits as well as separate antibodies to be used in their own proprietary machines.[29] All of Centocor's diagnostic tests were designed to be compatible with existing diagnostic systems that allowed for both the testing and analysis of results, such as those marketed by Abbott and Roche and used by the majority of clinical laboratories.[30] In this way Centocor became seen as a collaborator rather than a competitor in the diagnostics space.

An important catalyst in Centocor's early success was its swift winning of regulatory approval for two diagnostic tests: one for gastrointestinal cancer (using an antibody licensed from the Wistar) and the other for hepatitis B (developed by Zurawski and licensed from the MGH). Both tests reached the market by 1983. Centocor's hepatitis B test was in high demand because from the early 1970s many countries, including the US, required the screening of blood intended for blood transfusion.[31] Between 1983 and 1986 Centocor introduced another three tests to the market: one for diagnosing ovarian cancer (licensed from the Dana Faber Cancer Institute), the first diagnostic tool available for the disease; a test for breast cancer (licensed from Scripps Clinic and Research Foundation); and another for colorectal cancer (licensed from the Wistar).[32] Centocor also developed the first antibody diagnostic test for multi-drug resistance, a major problem for cancer patients. By 1990 Centocor had captured more than a quarter of the world's market for antibody-based tests for cancer.[33]

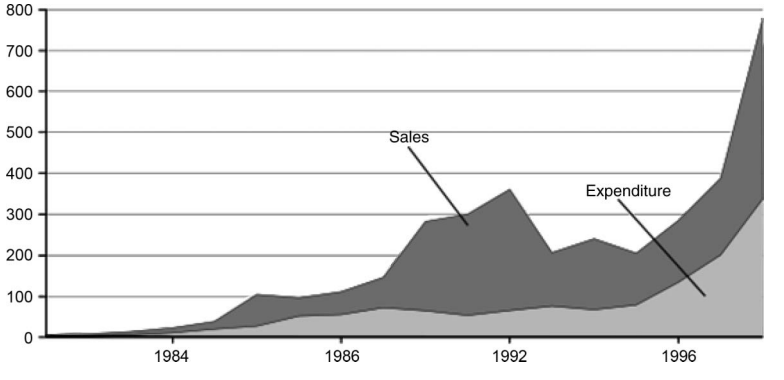

Figure 1. Centocor's revenue and expenditure 1982–98 (US$ million).
Source: Centocor, *A/Rs*.

Between 1979 and 1985 Centocor's team built up a profitable business with revenues of just under US$50 million (Figure 2). It was highly lucrative because most of the bottom-line revenue came from royalties.[34] By 1987 Centocor was one of the very few monoclonal antibody companies with earnings.[35]

Finance: 'grab as many cookies as you can'

Just as fundamental as partnering was to Centocor's early success was Wall and Schoemaker's ability to find capital. Between 1979 and 1981 they raised approximately US$7 million through private placements of its stock. In December 1982 Centocor had its first public offering, raising US$21 million. Centocor was the third company in the biotechnology industry to go public. The first company had been the Californian-based company Genentech, promoting products using recombinant DNA, which raised US$35 million in 1980. Cetus, another Californian biotechnology company set up in 1971, was the second company, raising US$107 million in 1981.[36] Centocor raised further cash from public offerings in 1983, 1986, 1990 and 1991, the last raising US$100 million.[37]

Wall and Schoemaker also secured funds through R&D limited partnerships. First used by Delorean Car Company in 1975, R&D partnerships allowed companies to raise capital from private individual investors for specific research projects off the balance sheet, providing investors with tax benefits and potentially higher returns than equity investments.[38] Genentech was the first biotechnology company to use the mechanism, in 1982, using it to develop human growth hormone and gamma interferon drugs.[39] Centocor was one of the most successful and aggressive users of R&D limited partnerships within the biotechnology industry, establishing at least four such partnerships between 1984 and 1987.[40]

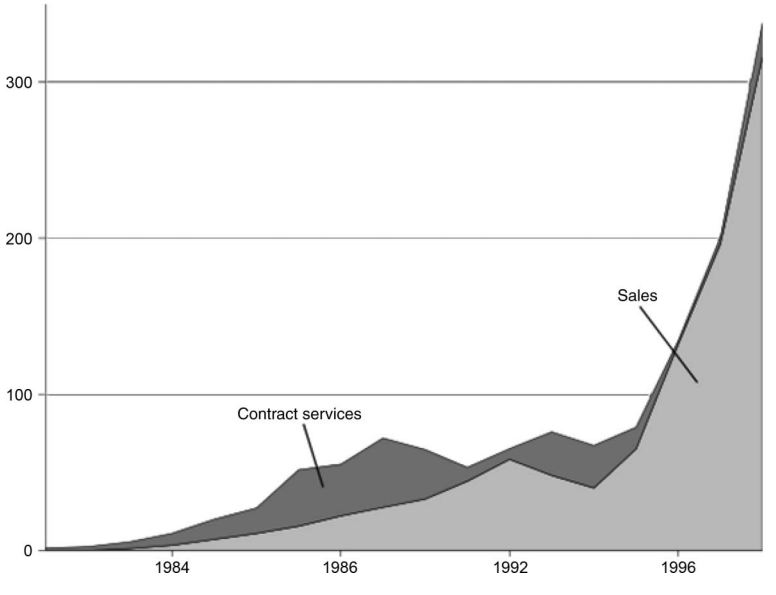

Figure 2. Centocor's revenue: sales and contract services 1982–98 (US$ million).
Source: Centocor, *A/Rs*.

Central to Centocor's fundraising was Schoemaker's philosophy that it should not be driven by the company's business plan. He believed that even if Centocor had a lot of money on the balance sheet more money should be raised whenever the opportunity arose. As he explained,

> In Centocor's early days, Bill Hambrecht of Hambrecht and Quist[41] advised me: 'When the cookie jar comes around, grab as many cookies as you can because you'll never know when it comes around again.' He also advised me to discard all of the traditional business evaluations such as cash flow, price/earnings, etc. in deciding when and how much money to raise. He told me that each week he had five CEOs in his office who had insufficient capital and that he had never had a CEO come to him and tell him he had too much money.[42]

Figure 3 shows Centocor's assets, including investments, 1982–98.

Centocor expands its horizons

While initially funnelling resources into blood-based diagnostics, Wall and Schoemaker quickly looked for ways to expand into the therapeutics sector. Therapeutics posed greater uncertainties than diagnostics. Much of the commercial attention in the nascent biotechnology therapeutics industry was focused on using recombinant DNA technology for the production of drugs for which there were existing therapeutic models and markets.[43] Therapy based on mabs was a novel idea and remained uncharted territory.

Using mabs for therapeutic purposes presented considerable new challenges. Unlike the blood-based diagnostics that Centocor had heretofore been developing, which involved the deployment of mabs in tests on blood removed from the human body, therapeutics required the administration of mabs directly into the human body. Monoclonal antibody drugs therefore posed greater safety concerns. Therapeutics also needed far larger numbers of mabs than needed for diagnostics, raising additional manufacturing and quality control challenges.[44]

Early on, Wall and Schoemaker recognised that the time and cost required to bring therapeutic products to market exposed their newly emerging company to unacceptable financial risks, and could divert resources and hinder innovation. In

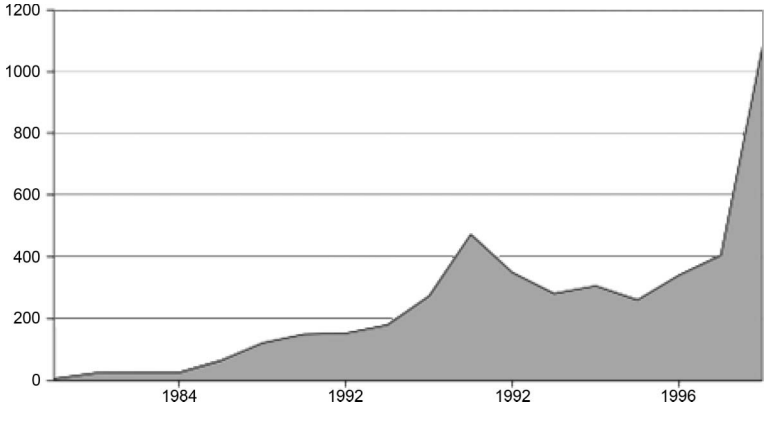

Figure 3. Centocor's assets 1982–98 (US$ million).
Source: Centocor, *A/Rs*.

order to minimise the risk and gain financial, scientific and technical resources as well as credibility they therefore devised a strategy to generate relationships with leading companies. By 1983 Centocor had established collaborations with two companies for this purpose: the American chemicals company FMC Corporation and the Swiss-based pharmaceutical company F. Hoffman-La Roche.[45]

Centocor's alliance with FMC began in 1980, with FMC agreeing to contribute a total of US$12.4 million. Split 50/50 and managed by a committee with a representative from each company, each partner had the option to purchase all of the other's interest in the joint venture.[46] One of the aims of the collaboration was to find a way to produce mabs from cell-lines more closely resembling human antibodies. This was particularly important if Centocor was to gain leadership in the mab therapeutics field. Most of the early mabs developed from the time of Kohler and Milstein were derived from mouse cells. These mabs had certain drawbacks: a short half-life and poor recognition by receptors in the human body necessitated administration in high doses which posed greater potential for life-threatening allergic reactions and viral safety problems. For Centocor human antibodies not only promised greater safety and efficacy for therapeutic products[47] but provided a competitive advantage in securing investment.[48] In 1986 Centocor gained exclusive rights to the human antibody technology developed through the venture. In return FMC received 1.35 million of Centocor's shares.[49] The only other biotechnology company that had managed to develop human antibodies by then was Cetus.[50]

In furthering its credibility in the therapeutic sector Centocor devised a strategy to develop mabs as contrast agents for imaging procedures. While not therapies in themselves, the use of mabs as imaging agents tested the safety of mabs for potential therapies and provided useful aids for the evaluation and therapeutic treatment of a patient. In 1985 Centocor established an *in vivo* diagnostic imaging unit and began to develop three products directed towards imaging diseases and conditions of the cardiovascular system. The market for mab imaging diagnostic products was expected to be between five and ten times larger than that of blood-based diagnostics.[51] By 1987 Centocor had an alliance with Ortho Biotech, a division of Johnson & Johnson, to distribute and market the imaging products in the US and elsewhere.[52] In August 1989 Centocor won European approval for its imaging product, Myoscint, which began to be marketed in France, Germany, Italy, Spain and the United Kingdom. The same product won American approval in 1996. Licensed originally from MGH, Myoscint could locate and estimate the amount of dead heart tissue from a heart attack.[53]

Centocor goes it alone

In 1986 Wall and Schoemaker decided that while they would continue to develop therapeutic products though joint ventures, the profits generated from the highly successful blood test business and contract revenue from technology licensing, and selected product marketing arrangements could be used to build Centocor into a major pharmaceutical company such as Merck by the year 2000.[54] Transforming Centocor into a globally integrated pharmaceutical company was not an unusual goal for the time. Other executives from leading biotechnology companies were pursuing the same vision with some success. In 1985 Genentech launched Protropin to treat growth hormone deficiency in children. It was the first recombinant pharmaceutical product to be manufactured and marketed by a biotechnology company without the help of a partner.[55]

By 1988 Centocor's research group had identified 30 new entities for possible drug development and had 12 Investigational New Drug Applications filed with the US Food and Drug Administration (FDA), many of which were mabs, and had clinically evaluated 10 products.[56] While many of Centocor's competitors at this time were focusing on deploying mabs for cancer treatment and Centocor had its own cancer programme,[57] Centocor's preferred lead candidate was an antibody targeting septic shock, a deadly disease usually acquired in hospitals and traditionally treated, ineffectively, with antibiotics. By 1986 Centocor had two human antibodies, one developed in-house through collaboration with FMC, and one licensed in from the University of California San Diego, known as HA-1A.[58]

At least a third of septic shock cases are caused by gram negative bacteria, a class of bacteria that possesses a unique outer membrane that hinders cell penetration by antibiotics and other drugs. During the 1980s gram negative sepsis was the third leading cause of death in the US, with over 100,000 people dying from the condition each year, accounting for up to US$10 billion in health care expenditures annually. Wall and Schoemaker believed that should Centocor develop a drug to combat a critical medical problem they would have a major blockbuster. The estimated market for products to treat septic shock in 1990 was over US$300 million.[59]

In order to maximise the potential of HA-1A, trade-named Centoxin, Wall and Schoemaker, in part encouraged by Wall Street advisors, decided that rather than selling the rights to the drug to another company they would develop and market Centoxin internally. This they believed would give them greater control over the product and larger revenues.[60] As Tony Evnin, one of Centocor's first investors and directors, explained,

> At that point in time it seemed like such an important product and it was a product in a new area. We wanted the ability to keep it all to ourselves. Perhaps we were a bit greedy, but it seemed like it was something that, by bringing in … additional talent [from the pharmaceutical industry], we could take on ourselves.[61]

One of the reasons Wall and Schoemaker decided to develop and market Centoxin internally was that it would help build the necessary infrastructure for becoming an integrated pharmaceutical company.[62] This, however, required major upscaling of the company's manufacturing capabilities and marketing involving large sums of cash. At least US$150 million was needed to get Centoxin to market. Between 1986 and 1992 Centocor went through nine different equity, debt and off-balance sheet financings, netting more than US$500 million. By 1992 US$450 million had been spent on clinical trials and building a sales force of 275 people (200 in the US and 75 in Europe) and building two new factories: one in Holland and one in the US.[63]

Heeding advice from Wall Street, Wall and Schoemaker also restructured the management team to bring on board skills in pharmaceutical development, regulation and marketing by the hiring of staff from large pharmaceutical companies. In December 1987 James Wavle, former president of Parke-Davis, Warner-Lambert's pharmaceutical unit, became Centocor's president and chief operating officer. Working alongside Schoemaker, who retained his position as chief executive officer and replaced Wall as chairman, Wavle had the responsibility of turning Centocor into a globally integrated pharmaceutical company.[64] The recruitment of pharmaceutical executives had a major impact on the culture within Centocor, bringing in new management styles, more aggressive marketing and a higher cash burn.[65]

Confidence was high that Centoxin would succeed. Such optimism was not unfounded. In February 1991 a leading American journal ran an article indicating Centoxin reduced gram-negative sepsis by 39%. For those who went into septic shock the drug reduced mortality by 47%.[66] The same month the US army administered the drug to soldiers fighting in the first Gulf War.[67] A month later the European drug regulatory body approved Centoxin for the treatment of gram negative sepsis. Six months later, in September 1991, a FDA panel advised approval of Centoxin to treat septic shock.[68] Centocor's sales were predicted to soon be in excess of US$1 billion. On this basis Schoemaker believed Centocor would have more than 50% of the share of the antibody pharmaceuticals market in Europe, the US and Japan by 2000.[69]

'Centocorpse': Centocor in crisis

The good news, however, did not last. In late October 1991 an American federal court ruled that Centocor's patent for Centoxin infringed one held by Xoma Corporation, a competitor biotechnology company based in California developing a similar drug for septic shock in partnership with the pharmaceutical company Pfizer Inc.[70] Centocor's executive was unsure how they should handle the matter. This was the first major case of litigation they had experienced. Initially Schoemaker wanted to settle, but Wavle persuaded him to fight based on the belief that a settlement could result in cross-licensing and thereby a loss in revenues. The hope was Centocor could strike lucky like the biotechnology company Amgen had done in its patent dispute with Genetics Institute.[71] In retrospect, Schoemaker believed his decision not to settle the dispute with Xoma was one of his biggest strategic errors.[72] Losing the patent battle to Xoma, the litigation cost Centocor dearly in terms of time and money and publicly aired questions about the design of Centoxin's trials and the data analysis.[73]

Adding to these problems from late 1991 some medical practitioners began to question the potentially high price of Centoxin (between US$3000 and US$4000 for each patient) and the degree to which they could predict which patients would most benefit from the drug.[74] By early 1992 initial European sales of the drug were also far below expectations. More pessimistic news was to follow when on 20 February 1992 the FDA requested additional information about Centoxin. Triggering shock in the financial community, the tidings sent Centocor's shares tumbling 19% or US$8.125 a share, closing at US$33.125 a share. Only two weeks before the stock had traded at US$50 a share. The slide in Centocor's share represented a US$675 million drop in its market value.[75]

Despite the negative publicity, Schoemaker believed the problems could be resolved. Three months later, however, on a public holiday in April, he received a telephone call at home from David Kessler, head of the FDA, indicating Centoxin would not be approved because of insufficient evidence to establish its efficacy and the necessity of more trials before it could be reconsidered for approval.[76] For Schoemaker, usually a great optimist, this news was 'the worst thing that could have happened'. The devastation was great for everyone in the company.[77]

Hitting media headlines on 15 April 1992, the news stunned investors. Nicknamed 'Centocorpse' by Wall Street, Centocor's stock dropped 41% in one day.[78] In the week that followed, disgruntled investors filed six lawsuits against Centocor's executives alleging violation of federal securities laws and called for damages.[79] Shareholders had seen US$1.5 billion of Centocor's market

capitalisation disappear, its stock rate having fallen from a high of US$60 to just US$6.[80] Sensitive to the calamities of one of its leading companies, the biotechnology industry suffered its own financial aftershock with the news.[81]

Rescuing Centocor: shifting back to a model of collaboration

The FDA's decision had not killed Centoxin, but Centocor desperately needed time and money to rescue the drug, develop its other products and survive. With the future of the company at stake, Schoemaker and Wall immediately crafted a rescue strategy. To stop the company's cash burn they rapidly laid off hundreds of people, primarily the sales representatives hired for Centoxin's launch. Within a short period the company's employee base had shrunk by a quarter. The company's management team was also reshuffled: Wavle and other recent recruits from the pharmaceutical industry departed.

Crucial for the company's financial survival was also Schoemaker and Wall's reversion to collaboration. The income generated from the diagnostics division, which was bringing in millions of dollars, was insufficient to keep the company afloat and they could not rely on the investment community with the fall in Centocor's stock.[82] Within days of the FDA's announcement Wall and Schoemaker plunged into a frenzy of partnership and fundraising efforts with a number of pharmaceutical companies, including SmithKline Beecham and Eli Lilly.[83] Schoemaker's dynamism and optimism were a major factor in driving this forward.[84]

What Wall and Schoemaker had on their side were other promising products in Centocor's pipeline plus the fact that half the industry wanted to obtain Centoxin despite its problems. J.P. Garnier, who headed SmithKline Beecham at the time, recalled,

> We tried to convince Hubert [Schoemaker] to do a deal with us, and Centoxin turned into a bidding contest between several companies. . . . I remember a phone call coming in over the weekend saying, 'It's going to cost you one hundred million dollars in an upfront payment to get Centoxin now.' Now it doesn't sound impressive but it was the equivalent of saying a billion today. A hundred million was unheard of. Nobody had ever paid this kind of upfront money.

As Garnier explained,

> Hubert was a terrific salesman. He whipped up this asset into something that got to be very appealing. He packaged Centoxin very effectively and before you knew it, the bride looked sensational. Everybody was influenced by his sincere belief in the drug and what it could do.[85]

In July 1992 Centocor finalised a licensing agreement with Eli Lilly. Under the agreement Centocor received US$100 million upfront from Eli Lilly, an unprecedentedly large payment for the time. Half of this amount went towards Eli Lilly purchasing 2 million shares in Centocor, thereby giving it a 5% stake in the company. The other half went towards providing the much needed cash to continue developing and seeking clearance for Centoxin. In the event that Centoxin failed, Eli Lilly agreed to pay a further US$25 million towards the development of ReoPro, a cardiovascular drug that Centocor was currently developing clinically.[86]

In addition to providing access to capital, the alliance was strategically useful for Centocor because Eli Lilly had a significant presence in the antibiotics field and

a strong understanding of the US infectious disease market crucial for the further development of Centoxin. Eli Lilly was also more receptive to biotechnology than many pharmaceutical companies, having partnered with Genentech to launch the first genetically engineered insulin and having acquired Hybritech, Centocor's main competitor in mab diagnostics in 1986.[87] For Eli Lilly the alliance gave them a chance to enhance their knowledge in the application of mabs for infectious disease therapeutics and access to Centocor's European sales team, thereby opening up a new avenue for selling Lilly products.[88]

In the following months Eli Lilly and Centocor worked closely together, overseen by product committees established at both companies, on a new trial for Centoxin, launched in June 1992.[89] Despite Eli Lilly's support, in January 1993 Centoxin's development was abandoned because interim trial data indicated unexpectedly high mortality. The poor results were attributed to flawed trial design. Centoxin proved effective in treating septic shock stemming from gram negative bacteria, but this accounts for only about a third of patients who present with sepsis. No diagnostic tool existed, however, to detect which of the patients presenting in the trials had gram negative sepsis. In the absence of a diagnostic tool Centocor's clinical team had insufficient data to convince the FDA of the drug's efficacy.[90]

Centocor turns profitable

Despite the setback with Centoxin, by early 1993 Centocor was financially turning a corner. Its cash burn had fallen from US$50 million to US$30 million between the first and last quarters of 1992. Part of this had been achieved through lay-offs, but it had also been helped by the reversion to collaboration.[91] Good results were also beginning to come from other products in Centocor's pipeline.

Some of the most cheering news was the positive data Centocor's clinical team was getting from the cardiovascular drug ReoPro. Licensed from State University of New York, Stony Brook, in 1986, much of the early development and testing of ReoPro had been undertaken by Centocor with funds raised from a R&D limited partnership set up in 1987.[92] By 1992, the time of the alliance with Eli Lilly, ReoPro was in phase III clinical trials and Centocor was planning to file for FDA and European regulatory approval the following year.[93]

In early 1993 when the first results from the drug's trial emerged positive it was clear not only that Centocor possessed a marketable drug but its future was now secure.[94] Submitted for approval in 1993, ReoPro took just 10 months to be approved by the European regulatory authorities and 12 months by the US FDA. These approvals came through in December 1994. ReoPro's approval marked a key milestone for Centocor and placed mabs firmly on the therapeutic map, showing for the first time that they could be used for acute conditions. The drug was the third monoclonal antibody to win approval as a therapeutic, the first two having been approved in 1986: Johnson & Johnson's Orthoclone OKT3 (used to prevent kidney transplant rejections) and Burroughs Wellcome's Digibind (used to mop up any dangerous excess of the heart attack drug digitalis).[95] The first therapeutic product ever to receive simultaneous US and European approval, ReoPro was the only new biotechnology product sanctioned in 1994. In December 1995 ReoPro's marketing potential was further boosted when clinical trials showed it effective for unstable angina, broadening its potential market to more than 1 million patients.[96]

Centocor's partnership with Eli Lilly was crucial to the development of ReoPro. While Centocor had undertaken and financed internally much of the early development and clinical trials, the alliance with Eli Lilly provided the necessary time to do the further work.[97] Under the alliance agreement, Eli Lilly exercised its right to market the drug in the US and most of Western Europe. ReoPro rapidly became a success, with worldwide sales of US$23 million in its first year, 1995. By 1999 worldwide sales had increased to US$447.3 million. Four years later the drug was being investigated for non-cardiac indications, including sickle-cell anaemia and cancer.[98]

Following ReoPro's success, Centocor's team soon had another major breakthrough with a drug called Remicade. The drug, based on an antibody called cA2, originated from a collaborative research and development agreement established in January 1984 between Centocor and the laboratory of Jan Vilcek, a scientist based at New York University School of Medicine.[99] Initially Centocor's researchers investigated cA2 in-house alongside Centoxin to combat sepsis, but clinical studies showed it more promising for treating autoimmune disorders. In 1998 Centocor won FDA approval for Remicade, to treat Crohn's disease. A year later Remicade was approved for rheumatoid arthritis. Today the drug is a major blockbuster drug and has received approval in 88 countries for 15 inflammatory disease indications and is being used to treat over 1 million patients worldwide. In 2006 the drug generated US$3.77 billion in worldwide sales.[100] The approval of Remicade marked a significant point in the development of mabs as therapeutics, showing for the first time that mabs could be deployed for chronic conditions.

The approval of ReoPro and then Remicade signalled how far Centocor had come from its humble beginnings as a company specialising in mab diagnostics. By 1999, 20 years after its founding, Centocor had raised US$1.5 billion and brought to market 10 products.[101] Despite the success, Schoemaker and David Holveck, Centocor's chief executive officer, realised their company could no longer remain independent if it was to go forward as a serious player. The cash they had secured was insufficient for maintaining and growing the company's research and development programme and expanding the company's manufacturing and marketing capabilities. They also recognised that having become so successful the company could be subject to a takeover bid. In order to prevent a hostile bid, in 1998 they began to assess the company's value and identify possible partners.[102] A year later Holveck and Schoemaker secured a deal for US$5.2 billion, making Centocor a subsidiary of Johnson & Johnson. The deal allowed Centocor to continue to operate independently while benefiting from the infrastructure, financial resources and credibility of a large pharmaceutical company. Within three years of the deal Centocor more than doubled its workforce, from 1200 people to 2800 worldwide, and more than tripled the number of new drug candidates entering late-stage testing, many in disease areas Centocor had not explored before, including diabetes, organ transplant rejection and asthma.[103]

Conclusion

Centocor's history is illustrative of the important role collaboration has played in the building up of the biotechnology industry. A key lesson from Centocor's history is how important research and development partnerships can be to a young company just beginning to create a portfolio and how critical alliances with established

companies can be to breaking into a competitive marketplace. Coming unstuck when straying away from collaboration, the story of Centocor is a salutary reminder of the risks for newly emerging companies of going it alone.

Centocor's experiences with collaboration and attempts to go it alone, however, are not universal in the biotechnology industry. Plenty of collaborations between biotechnology companies and large pharmaceutical companies have failed in the past and continue to do so to this day. Amgen, a biotechnology company founded just one year after Centocor, landed up in a costly court case over its patents and experienced huge financial losses as a result of the marketing partnership it formed in 1985 with Johnson & Johnson, for its first drug erythropoietin, a treatment for anaemia.[104] The company had more success when it decided to develop and market its second drug Neupogen, a treatment for neutropenia, independently.[105] The contrast between Centocor and Amgen shows how idiosyncratic the risks and outcomes can be for biotechnology companies when deciding to collaborate or go it alone. This is highly influenced by the personalities involved, market conditions, scientific and technical developments, and the cultural fit between organisations.

Acknowledgements

The author would like to thank Anne Faulkner Schoemaker for allowing generous access to Hubert Schoemaker's personal files and reading the draft of this paper. Grateful thanks also go to Stelios Papadopoulos, Alison Kraft and David Holveck for providing insightful comments on initial drafts of the paper. Much appreciation also goes to all the people who agreed to be interviewed for this research supported by the Chemical Heritage Foundation.

Notes

1. Research for this paper is based on Centocor's company papers and the personal papers of Hubert Schoemaker (hereafter HS-PP) kindly provided by his widow Anne Faulkner Schoemaker and on oral interviews with Centocor's employees undertaken by the author in collaboration with the Chemical Heritage Foundation which houses the interview transcripts. The author conducted all interviews listed below except where specified.
2. For a history of the biotechnology industry see Gambardella (1995, chaps. 2–3) and Chandler (2005, chap. 10).
3. For Koprowski's biography see Vaughan (2000).
4. HS-PP: Centocor, Centocor Oncogene Research Partners LP, 9 June 1984.
5. HS-PP: M.A. Wall and E.C. Allen, 'Investment prospectus: Medical diagnostic business', date unknown.
6. Eichmann (2005); Cambrosio and Keating (1995).
7. Vaughan (2000, pp. 174–177).
8. H. Koprowski and C. Croce, 'Method of producing tumor antibodies', US Patent 4,172,124 (filed 28 April 1978, issued 23 October 1979); H. Koprowski, W. Gerhard, and C. Croce, 'Method of producing antibodies', US Patent 4,196,265 (filed 15 June 1977, issued 1 April 1980). Boehringer Ingelheim, a large German chemical/pharmaceutical company turned down the patents for US$500,000 per year for 10 years (Vaughan, 2000, p. 179).
9. Interview with Vincent Zurawski by Ted Everson (4 January 2007).
10. HS-PP: Wall and Allen, 'Investment prospectus', p. 30.
11. Interview with Tony Evnin, Venrock Associates partner and Centocor director (1981–99) by author and Ted Everson (14 September 2006).
12. HS-PP: Wall and Allen, 'Investment prospectus', p. 6.
13. HS-PP: Wall and Allen, 'Investment prospectus', pp. 28, 31; 'A medical marvel' (1983); 'Biotechnologists are ready' (1981); 'Smart bombs of biology' (1981).
14. 'A medical marvel' (1983); Hamilton (1983); for other companies developing mabs see Jones and Kraft (2004).

15. Vaughan (2000, p. 179) and interviews with Koprowski by author and Ted Everson (13 July 2006) and Michael Dougherty (23 January 2007). Dougherty was Centocor's assistant controller, treasurer, chief financial officer and senior vice president (1983–93).
16. Interview with Evnin; HS-PP: L.F. Rothschild et al., *Centocor Inc: Prospectus for public offering* (22 July 1983, p. 21); Teitelman (1985).
17. Interview with former NCI researcher and Centocor collaborator Robert Gallo (11 July 2006). See also interview with Sarah Cabot, Centocor's technology licensing director (1986–90), by Jennifer Dionisio (7 November 2007).
18. Interviews with Evnin and Anne Faulkner Schoemaker (10 July 2006). See also HS-PP: Centocor, *Annual report* (1983, p. 6). Hereafter all Centocor's *Annual reports* (*A/Rs*) are contained in HS-PP.
19. Schoemaker, cited in Vaughan (2000, p. 186) and interview with Faulkner Schoemaker.
20. HS-PP: L.F. Rothschild et al., *Centocor Inc: Prospectus for public offering* (14 December 1982, pp. 19 and 25). Stanley Cohen and Herbert Boyer faced similar hostility to the commercialisation and patenting of their technology and founding of Genentech (see Smith Hughes, 2001).
21. Vaughan (2000, pp. 182–186).
22. Interview with Gallo; Schoemaker, cited in Vaughan (2000, p. 186).
23. Before the Bayh-Dole Act universities wishing to obtain a patent arising from federally funded research required permission from federal authorities to do so (see Smith Hughes, 2001, p. 551).
24. Centocor, *A/R* (1985, p. 5); HS-PP: Rothschild, *Centocor Inc*. (1983, p. 22); Momich (1990, p. 31).
25. Interviews with Koprowski and Zurawski.
26. Dickinson (1990, p. 3).
27. HS-PP: Wall and Allen, 'Investment prospectus', p. 6.
28. Centocor, *A/R* (1985, p. 27).
29. Interview with Holveck.
30. HS-PP: Rothschild, *Centocor Inc*. (1982, p. 15; 1983); Centocor, *A/Rs* (1983, p. 2 and 1985, p. 15); correspondence between author and David Holveck, November 2007; interview with Holveck by author and Ted Everson (14 July 2006). Holveck was Centocor's head of diagnostics from 1983 and Centocor's chief executive officer from 1992.
31. Interview with Holveck; Fishlock (1983); Dickinson (1990, p. 3); Centocor, *A/R* (1983, p. 14); 'FDA approved' (1984); Momich (1990, p. 31).
32. HS-PP: Centocor Press Release, 'Centocor receives FDA panel recommendation to approve ovarian cancer test', 3 November 1986; Thompson (1987).
33. Interview with Zurawski; 'TWST names' (1987); Centocor, *A/R* (1990, p. 14).
34. HS-PP: H. Schoemaker, 'Wharton talk', 17 April 2000 and interview with Holveck.
35. Bylinsky (1987).
36. Bugos (2001).
37. HS-PP: Rothschild, *Centocor Inc*. (1982, 1983); HS-PP: PaineWebber, *Centocor, common stock* (13 December 1985, p. 7); Centocor, *A/Rs* (1986, 1987, p. 2 and 1990, p. 3).
38. Interviews by author and Ted Everson with PaineWebber investment bankers Stephen Evans-Freke (14 September 2006) and Stephen Webster (13 July 2006) and by author with Bruce Peacock, Centocor's chief financial officer 1981–92 (10 July 2006). See also Schiff and Murray (2004).
39. Bugos (2001).
40. Interviews with Evans-Freke and Webster. See also HS-PP: Centocor, *Centocor Oncogene research partners LP*; PaineWebber, *Centocor common stock*, p. 22; PaineWebber, *Tocor II and Centocor prospectus* (21 January 1992), p. 5; Centocor, *A/Rs* (1985–88 and 1989, p. 31).
41. Bill Hambrecht, co-founder of Hambrecht and Quist in 1968, an investment bank specialising in emerging high-growth technology companies, was one of Genentech's early investors. See Bugos (2001, p. 28).
42. HS-PP: Schoemaker, 'Wharton talk'.
43. For more on the development of recombinant insulin see Hall (1987).

44. Interview with Centocor's vice president of pharmaceutical development (1988–93) Renato Fuchs (1 July 2008). See also Bylinsky (1987).
45. Centocor, *A/R* (1983, p. 6).
46. Centocor, *A/Rs* (1983, pp. 18, 28; 1985, p. 2); HS-PP: Rothschild, *Centocor Inc*. (1983, p. 47).
47. Centocor, *A/R* (1986).
48. Interview with Evans-Freke.
49. Centocor, *A/R* (1986, p. 3).
50. Bylinsky (1987).
51. Bylinsky (1987).
52. Centocor, *A/R* (1988).
53. HS-PP: PaineWebber, *Centocor common stock* (1985, pp. 4, 6, 340); PaineWebber, *Tocor II*; Centocor, *A/R* (1990, p. 7). Centocor SEC filing Form 10-K for the year ending 31 December 1995; Pollack (1989). Interviews with Holveck, Harlan Weisman (30 November 2006) and Jeffrey Mattis (22 February 2007). Harlan Weisman was Centocor's president of R&D and team leader for ReoPro development (1990–99) and Mattis was Centocor's vice president of pharmaceutical development (1979–98).
54. Centocor, *A/Rs* (1986, p. 17; 1988, p. 5); Dickinson (1990, p. 2).
55. Bugos (2001); interview with Fuchs.
56. Centocor, *A/R* (1988, pp. 2, 12).
57. Interview with Centocor's vice president of clinical research and medical research (1990–97), Richard McCloskey (19 January 2007).
58. Centocor, *A/R* (1985, p. 29). Interviews with Centocor's development project manager (1983–99), Denise McGinn (12 September 2006), and Holveck, Zurawski and Fuchs.
59. Momich (1990, pp. 26–28).
60. Interview with Philadelphia-based market analyst, Bernard Schaffer (11 September 2006).
61. Interview with Evnin.
62. Interview with Fuchs.
63. Winslow (1991); Dickinson (1990); Longman (1992, p. 24).
64. 'Centocor Inc.' (1986).
65. Interviews with Holveck, Peacock and Cabot. Joint interview with Sandra Faragalli, Patty Durachko and Ray Heslip (12 September 2006). All three were long-time employees of Centocor, working in the administrative, finance, warehouse and shipping sections. Interview with Centocor's vice president of diagnostics operations (1985–98), Paul Touhey by author and Ted Everson (15 September 2006).
66. Ziegler et al. (1991).
67. 'Blasting bacteria' (1991); 'Centocor Inc.' (1991).
68. Usdin (1992); Shaw (1992a); 'FDA snag' (1992); Valeriano (1992); Newman and Pettit (1992).
69. 'Centocor Inc.' (1991).
70. Patent disputes were common in the industry and could be devastating for the companies concerned. See for example the case of CellPro which became bankrupt after failing to win a patent dispute as described in Bar-Shalom and Cook-Deegan (2002).
71. Interviews with Centocor's attorney (1987–99), George Hobbs (30 September 2006), PaineWebber investment banker (1987–2000) Stelios Papadopoulos (19 October 2006); and chief executive officer of Cephalon, Frank Baldino by author and Ted Everson (14 July 2006). Amgen and Genetics Institute's patent dispute started in 1988 and ended in May 1993 with the Genetics Institute paying Amgen US$15.9 million. Amgen SEC filing: Form:10-Q, 8/10/1994. Retrieved 14 July 2008, from http://sec.edgar-online.com/1994/08/10/00/0000318154-94-000020/Section10.asp
72. Interviews with Faulkner Schoemaker and Schaffer.
73. Interviews with Holveck and Papadopoulos. Centocor, *A/R* (1991, pp. 38–39); Valeriano, (1992); Fisher (1992).
74. Hinds (1992); interviews with Peacock, Holveck and Papadopoulos.
75. Usdin (1992); Shaw (1992a); 'FDA snag' (1992); Valeriano (1992); Newman and Pettit (1992); Longman (1992, p. 25).
76. Interview with Schaffer.

77. Interviews with Faulkner Schoemaker, Holveck, Faragalli, Durachko and Heslip.
78. Shaw (1992b); see also interview with Papadopoulos.
79. 'FDA: Centoxin data insufficient' (1992); Shaw (1992b); interview with Holveck.
80. HS-PP: Schoemaker, 'Wharton talk'; Longman (1992, p. 23); interview with Holveck.
81. Usdin (1992); Longman (1992, p. 27).
82. Interview with Touhey.
83. HS-PP: Centocor, *CenTropics* (1/4, Fall 1992, p. 1).
84. Interview with Papadopoulos.
85. Interview with J.P. Garnier by Ted Everson (12 July 2006).
86. 'Lilly to acquire' (1992); HS-PP: Centocor, *CenTropics*.
87. 'Drug company' (1985); Fikes (1999).
88. Interview with Fuchs; HS-PP: Centocor, *CenTropics*, p. 1.
89. HS-PP: Centocor, *CenTropics*, pp. 2–4.
90. Interviews with Holveck, Papadopoulos and Centocor's head of human resources (1990–99) Michael Melore by Ted Everson (21 May 2007).
91. Centocor, *A/R* (1992, p. 7).
92. Centocor, *A/Rs* (1987–88).
93. Centocor, *A/R* (1992, p. 4).
94. Interview with McGinn.
95. Bylinsky (1987); Centocor, *A/R* (1994, pp. 2, 4); Cochlovius, Braunagel, and Welschof (2003); Farrell, Barnathan, and Weisman (2003).
96. *The New York Times*, 22 December 1995.
97. Interview with Holveck.
98. Eli Lilly and Co Inc, SEC Form 10-K, 30 March 2000. Retrieved 14 July 2008 from http://investor.lilly.com/EdgarDetail.cfm?CompanyID=LLY&CIK=59478&FID=950131-00-2201&SID=00-00. By 1998 competitor drugs were challenging the sales of ReoPro, including Aggrastat (Merck & Co Inc) and Integrilin (CorTherapeutics and Schering Plough). See SEC File 5-51443: Pharmainvest LLC – SC 14D1 – Painewebber R&D Partners, 3 March 1999. Retrieved 14 July 2008 from http://www.secinfo.com/dVut2.683s.b.htm; Loyd (2005); Cochlovius, Braunagel, and Welschof (2003); Brownlee (2004). In 2005 ReoPro earned US$104 million, four-fifths of the royalties earned by Stony Brook. See 'Stony Brook' (2007); Solnick (2006); Farrell et al. (2003, p. 343).
99. Interview with Jan Vilcek (12 July 2006). Vilcek is a microbiology professor at New York University School of Medicine.
100. 'Centocor drug' (2007).
101. HS-PP: Schoemaker, 'Wharton talk'.
102. Interview with Holveck; Knox (2000).
103. George (2002).
104. Moschol and Leiter (2001); for more on Amgen's development and marketing of Epogen see Goozner (2004, pp. 13–34).
105. Interview with Papadopoulos.

Notes on contributor

Lara Marks is a visiting senior research associate at Cambridge University and associate lecturer for the Open University. She has written and published extensively in the field of medical and scientific history, most notably her book *Sexual chemistry: A history of the contraceptive pill* (Yale University Press, 2001). Currently she is working on the history of the development of monoclonal antibodies as diagnostic and therapeutic tools and the rise of the biotechnology industry.

References

A medical marvel goes to market. (1983, April 11). *Business Week*, 56.
Bar-Shalom, A., & Cook-Deegan, R. (2002). Patents and innovation in cancer: Lessons from CellPro. *The Millbank Quarterly*, *80*(4), 637–676.
Biotechnologists are ready to market another trick. (1981, February 7). *The Economist*, p. 87.
Blasting bacteria. (1991, February 25). *Times Magazine*.

Brownlee, C. (2004). Biography of Barry S. Coller. *Proceedings of the National Academy of Science USA*, *101*(36), September 7, 13111–13113.
Bugos, G.E. (2001). Interview with Fred A. Middleton, First Chief Financial Officer at Genentech, 1978–1984. Retrieved July 24, 2008, from http://content.cdlib.org/xtf/view?docId=kt8k40159r&brand=calisphere&doc.view=entire_text
Bylinsky, G. (1987, April 27). Coming: Star Wars medicine. *Fortune*.
Cambrosio, A., & Keating, P. (1995). *Exquisite specificity: The monoclonal antibody revolution*. Oxford: Oxford University Press.
Centocor drug marks milestone. (2007, November 6). *Philadelphia Business Journal*.
Centocor Inc. (1991, May 27). *The Wall Street Transcript*.
Centocor Inc. Chief Hubert Schoemaker adds chairman's post. (1986, December 2). *The Wall Street Journal*.
Chandler, A. (2005). *Shaping the industrial century: The remarkable story of the evolution of the modern chemical and pharmaceutical industries*. Cambridge, MA: Harvard University Press.
Cochlovius, B., Braunagel, M., & Welschof, M. (2003). Therapeutic antibodies. *American Chemical Society: Modern Drug Discovery* (October).
Dickinson, S. (1990, May 14). Biotech's Centocor jockeys for position in drug field. *The Scientist*, *4*, 1–5.
Drug company buys antibody firm – Eli Lilly and Co. buys Hybritech Inc. (1985, October 5). *Science News*. Retrieved July 10, 2008, from http://findarticles.com/p/articles/mi_ m1200/is_v128/ai_3969472
Eichmann, K. (2005). *Kohler's invention*. Basel: Birkhauser Verlag.
Farrell, C., Barnathan, E., & Weisman, H.F. (2003). The evolution of ReoPro clinical development. In K. Dembowsky & P. Stadler (Eds.), *Novel therapeutic proteins: Selected case studies* (pp. 323–346). Weinheim: Wiley-VCH Verlag GmbH.
FDA approved the first hepatitis-B monoclonal assay. (1984, June 27). *Chemical Week*, p. 96.
FDA: Centoxin data insufficient. (1992, April 15). *BioWorld Today*, *3*, p. 74E.
FDA snag and loss hurt Centocor stock. (1992, February 20). *The New York Times*.
Fikes, B. (1999). Why San Diego has biotech. *San Diego Metropolitan,* April. Retrieved July 1, 2008, from http://www.sandiegometro.com/1999/apr/biotech.html
Fisher, L.M. (1992, July 30). Centocor and Xoma settle patent fight. *The New York Times*.
Fishlock, D. (1983, October 24). Why Centocor gets the 20% it asks for: The 'Intel of biotechnology' stakes its claim. *Financial Times*, p. 14.
Gambardella, A. (1995). *Science and innovation: The US pharmaceutical industry during the 1980s*. Cambridge: Cambridge University Press.
George, J. (2002, August 16). Centocor now bigger than ever. *Philadelphia Business Journal*. Retrieved July 24, 2008, from http://philadelphia.bizjournals.com/philadelphia/stories/2002/08/19/story2.html
Goozner, M. (2004). *The $800 million pill: The truth behind the cost of new drugs*. Berkeley, CA: University of California Press.
Hall, S. (1987). *Invisible frontiers: The race to synthesize a human gene*. Oxford: Oxford University Press.
Hamilton, M.M. (1983, October 30). Competition feverish in health field: Immunodiagnostics in infancy. *The Washington Post,* Sunday final edition, p. G1.
Hinds, C.J. (1992, 18 January). Monoclonal antibodies in sepsis and septic shock. *British Medical Journal*, *304*, 132–133.
Jones, G., & Kraft, A. (2004). Corporate venturing: The origins of Unilever's pregnancy test. *Business History*, *46*(1), 100–122.
Knox, A. (2000, May 7). He is building on his success. *The Philadelphia Inquirer*.
Lilly to acquire marketing rights to Centocor drug. (1992, July 17). *The New York Times*.
Longman, R. (1992, May). The lessons of Centocor. *In Vivo: The Business and Medicine Report*.
Loyd, L. (2005, June 19). Coming of age. *The Philadelphia Inquirer*. Retrieved November 7, 2007, from http://rtc.revolt.org/node/177
Momich, B. (1990). Building something significant at Centocor. *Pennsylvania Technology*, (2nd quarter), 25–31.
Moschol, A., & Leiter, J. (2001). Perfect partnering. *Nature Biotechnology*, Supplement to 19, (July), BE21–BE22.

Newman, A., & Pettit, D. (1992, February 20). Biotech stock lead index 0.64% lower; Centocor plunges on worry over drug. *The Wall Street Journal*.
Pollack, A. (1989, August 28). The next wave of diagnostics. *The New York Times*.
Schiff, L., & Murray, F. (2004). Biotechnology financing dilemmas and the role of special purpose entities. *Nature Biotechnology*, *22*, 271–277.
Shaw, D. (1992a, February 20). FDA, Wall Street bring bad tidings to Centocor. *The Philadelphia Inquirer*, p. B11.
Shaw, D. (1992b, April 27). Centocor absorbs new blows. *The Philadelphia Inquirer*.
Smart bombs of biology. (1981, June 22). *Newsweek*, US edition, p. 59.
Smith Huges, S. (2001, April 21). Making dollars out of DNA: The first major patent in biotechnology and the commercialization of molecular biology, 1974–1980. *ISIS*, *92*, 541–575.
Solnick, C. (2006, April 21). Stony Brook University reaps millions annually from research. *Long Island Business News*. Retrieved November 7, 2007, from http://findarticles.com/p/articles/mi_qn4189/is_20060421/ai_n16156975
Stony Brook ranks 20th in the US in income from licensed technology. (2007). *Stony Brook Graduate Review*, *4*(2) (Spring). Retrieved November 7, 2007, from http://www.grad.sunysb.edu/newsletter/AUTM%20Rank%202005.htm
Teitelman, R. (1985, May 6). Searching for serendipity: Centocor combs university labs for technology. *Forbes*, p. 80.
Thompson, L. (1987, June 16). New test for ovarian cancer detects residual cells in the blood. *The Washington Post*.
TWST names award winners biotechnology. (1987, December 14). *The Wall Street Transcript*, *97*(11).
Usdin, S. (1992, February 20). Wall Street vents frustration at Centocor. *BioWorld Today*, p. 1.
Winslow, R. (1991, September 5). Centocor's new drug clears FDA panel, Xoma's put on hold; both stocks go wild. *The Wall Street Journal*, *217*(47).
Valeriano, L.L. (1992, February 20). Centocor stock slides on news of drug snag. *The Wall Street Journal*.
Vaughan, R. (2000). *Listen to the music: The life of Hilary Koprowski*. New York: Springer Verlag.
Ziegler, E.J., Fisher, C.J., Sprung, C.L., Straube, R.C., Sadoff, J.C., & Foulke, G.E. (1991, February 14). Treatment of gram-negative bacteremia and septic shock with HA-1A human monoclonal antibody against Endotoxin. A randomized, double-blind, placebo-controlled trial. The HA-1A Sepsis study group. *New England Journal of Medicine*, *324*(7), 429–436.