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How Strategic Alliances Work in Biotech

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By **Lawrence M. Fisher**

Independence and integration used to be hallmarks of strength for American corporations. Today they could be signs of weakness as companies large and small rush to spin intricate webs of strategic alliances.

With technology in a constant state of change, transforming one industry after another in its wake, no company can afford to hang on to the status quo for long. But neither can it predict with assurance which promising piece of technology will pan out, spinning off tomorrow's hot new product. Alliances are the places to hedge all bets.

Some alliances are between partners of like size, whether big or small, who have reason to come together on a particular project. But strategic alliances—to fill gaps in such growth factors as the ability to innovate and distribute products—often involve companies of unequal size, and it is their size itself that sometimes brings them together. Big companies are looking to sign up with small companies to tap into their cutting-edge research and entrepreneurial energy. Small companies are looking for the deep pockets and vast distribution networks that big partners offer. And both sides like the fact that they can start a relationship without tying the knot for all time.

In short, alliances are a less costly, less risky and more flexible way to acquire capabilities than are outright acquisitions. Acquiring a company, after all, means buying its weaknesses along with its strengths. A successful alliance can lead to an acquisition, and many do, but the likelihood of a good marriage is enhanced in these cases by a period of living together.

All kinds of companies have been trying each other out in this way since the Reagan Administration got the ball rolling by relaxing enforcement of the antitrust laws. United States companies have formed 20,000 alliances since 1988 alone, with the number growing at a rate of 25 percent a year.

But perhaps no one has been busier spinning new webs than companies that are in the business of drug discovery and development. The growth of strategic alliances between the small biotechnology upstarts of the industry and the giant pharmaceutical companies has been truly dramatic: 85 deals in 1993, 210 in 1994 and 376 in 1995.

Driven to align by market forces often beyond their control, the biotech and pharmaceutical companies have spun enough webs to serve as a virtual laboratory for the creation of alliances. A close examination of their experiences sheds light on both the potential benefits and the inevitable problems of the alliance process, offering useful lessons for companies in any fast-moving industry.



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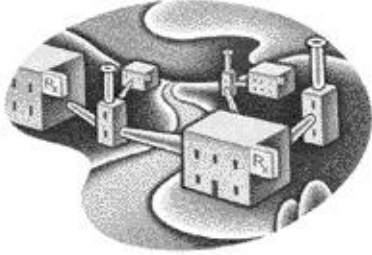


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It is simplistic to say that biotech companies are the product innovators and pharmaceutical companies the market deliverers, but it is along these lines that the two groups are coming together. Biotechnology, in effect, is becoming a supplier, selling its drug discovery capabilities to the pharmaceutical manufacturers. For their part, the drug companies are effectively "outsourcing" the R portion of R.&D., leveraging their development expertise with other companies' research.

Illustration by Josef Gast



"I think the industry we're creating is a feeder industry, maybe the first of its kind, with the exception of independent film making," said Stanley T. Crooke, chairman and chief executive of Isis Pharmaceuticals Inc. of Carlsbad, Calif., a leader in antisense technology, which seeks to treat disease at the genetic level. "What we're searching for, both pharmaceuticals and biotech alike, is a new model for the 21st century of what a company should look like."

But for those on either side of the equation, these relationships present a management challenge. Strategic alliances often involve partners that are not only sharply different in size but also have disparate corporate cultures, with widely divergent time frames for objectives that are themselves strikingly different.

"There's a real hurdle to clear when you have a sophisticated company dealing with a less sophisticated one," said John R. Harbison, a vice president for Booz-Allen & Hamilton in Los Angeles who specializes in strategic alliances. "It ends up being very difficult for both of them."

But when these deals are done right, they match strength to strength. And, in an increasingly cost-averse market, they can reduce redundancies in product development, manufacturing, marketing and sales.

"The world cannot afford inefficiencies anymore, so people cannot build organizations that duplicate things available out in the field solely for ego's sake," said Edward Penhoet, president and chief executive of the Chiron Corporation, the first biotech company to form multiple strategic alliances. "The company of the future will have fewer employees and more relationships."

Entering the 1980's, the large drug companies viewed biotechnology much the way mainframe computer manufacturers were then viewing the personal computer: interesting but hardly relevant.

The drug companies were so good at what they had been doing for so long, and the barriers to entry seemed so high, that the new technology of genetic engineering was seen at best as an addendum, at worst a distraction, so most ignored it. There were exceptions, notably Merck & Company, which began quietly developing its own biotech effort early on, but most companies stuck to the basic chemistry that had served them well for decades.



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Biotech, on the other hand, was full of the hubris of youth, charged by the truly astonishing advances made in the science of molecular biology, and energized by the same venture capitalists and investment bankers who had fueled the personal computer revolution. Biotech companies expected to supplant the drug makers, not collaborate with them, through the magic of laboratory manipulation of genetic material. While the early biotech firms all struck licensing deals with pharmaceutical companies, these were viewed for the most part as quick sources of cash and credibility, not as meaningful strategic relationships.

In retrospect, however, vast changes were occurring in their separate markets that would force the two groups, beginning in 1992, into each other's arms. For biotech, that was the year a few well-chronicled failures ended the stock market's love affair with their shares, closing that avenue of finance until mid-1995. For the large drug makers, 1992 was the year the Clinton Administration's proposals threatened to institutionalize the changes already wrought in the health care market by the move to managed care and the drive to contain costs.

Around the globe, managed care, market forces and health care reform legislation eliminated the drug companies' historic ability to continually raise prices on established products, or to profit from making near-copies of each other's drugs, charging proprietary prices for what essentially are generic products. Pharmaceutical companies suddenly found themselves under more pressure than ever before to produce innovative new drugs to maintain revenue growth, and alliances became the most efficient way to obtain them.

The sheer volume of deals in the last three years, as well as conventional wisdom, suggest that these are primarily marriages of convenience between cash-starved biotechs on the one hand and research-poor pharmas on the other. That is no doubt true of some of them, but it ignores the real strengths on both sides.

The biotech companies are research powerhouses, having successfully lured the best and brightest scientists away from academia for nearly two decades. The pharmaceutical companies excel in drug development, manufacturing and marketing, the very areas where their smaller rivals most often fall short. Moreover, the large companies have the resources to support the cost of developing a drug, an effort that can run into the hundreds of millions of dollars. They also have the patience to wait for a payoff. They know how long it takes to develop a drug, pass it through the required clinical trials and overcome the regulatory barriers.

But while nearly any well-endowed pharmaceutical company can pick and choose from a dozen or more proposed relationships with biotech concerns, an alliance entered that way is not likely to be strategic. It sounds obvious but still bears saying: a strategic alliance must relate back to a strategic plan. Companies must identify those areas in which they wish to acquire capabilities, rather than grow them internally. Then they must create a database of potential partners and seek out alliances with the best of them.

"Very few of the large companies have reconfigured themselves to have teams that can go out and identify value," said Richard Pops, president and chief executive of Alkermes Inc., a biotech company in Cambridge, Mass., that specializes in drug delivery technologies and has partnered with several larger concerns. "You need a team or an individual empowered to go out and make things happen, as opposed to a reactive organization that waits for things to come over the transom and then decides if they suit its core competencies."



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That has become all the more true now that biotech has blossomed in many directions. It used to mean one thing: therapeutic proteins, the production of genetically engineered copies of naturally occurring proteins for use as drugs. Biotech now encompasses a potpourri of research-based methods for drug discovery: antisense, carbohydrates, liposomes, gene therapy, combinatorial chemistry and genomics. Even if a pharmaceutical company invested heavily in recombinant D.N.A., the basic tool for producing therapeutic proteins, it probably has not made similar commitments to these other areas, any one of which could be critical to its future.

"In the new environment, where the payer makes the ultimate buying decision, only new drugs meeting unmet needs can demand the premium necessary to support research," said Martin Kuhn, head of new businesses for Ciba-Geigy A.G. in Basel, Switzerland. The payer is the managed care provider, which dictates the drugs doctors may prescribe. "The other thing is," Mr. Kuhn added, "with the explosive growth of new technologies, even a big company cannot afford to cover all the fields. We have identified fields where we need to complement our own skill base by tapping third parties' capabilities."

In most cases, Ciba has preferred to form alliances, rather than acquiring companies or technologies outright, in the belief that independence fosters scientific innovation and creativity. "You have to let the project management--determined by both sides--work with a high degree of operational autonomy," Mr. Kuhn said. "If you tell them too many times how to reach objectives, they will lose motivation."

A common element to successful strategic alliances, biotech and drug company executives agree, is that they are true collaborations. That means operational managers and scientists from both companies sharing data, experimentation and risks.

"In the early days, the biotech companies would do all the work, get checks from the pharma companies and throw data at them; it's easy to lose sponsorship that way," said Mr. Pops of Alkermes. "You have to have scientists working together; it has to be more than a financial relationship. It has to do with ownership of the project in big companies; unless you have a champion in the company, it's easy to slip off the agenda."

One essential ingredient in true collaborations that is not always easy to come by is mutual respect. The biotech companies typically were founded, staffed and managed by scientists, who may view the large drug concerns as stuffy, hierarchical and complacent. As Arthur Levinson, president and chief executive of Genentech Inc., put it, "The second- or third-rate people ended up in pharmaceutical companies, doing research." For their part, executives at major drug companies have too often dismissed the biotech concerns as a bunch of cloners producing proteins of scientific interest, but little commercial potential. Mutual respect has to be learned.

"The biotech side must believe that the major is not just a dumb source of money," said Dr. Daniel Vasella, president and chief executive of Sandoz Pharma, the pharmaceutical unit of Sandoz A.G. in Basel. "The biotech companies managed by an ex-major executive understand much better what is going on."

They may understand, but once they join the small company their own concerns and motivations change, making the management of these alliances no less stressful. For the executive of the small company, survival is always the key issue.

"If you have two companies that support each other, that complement each other, you can have a very happy coexistence," said P. Roy Vagelos, chairman of Regeneron Pharmaceuticals Inc., a biotech company specializing in neurological diseases, and the former chief executive of Merck. "But only if a company can retain a major product, that it can go all the way with, do you have the promise of being a real company. If you parcel out your future, your future is limited."



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One stumbling block to successful alliances is the vastly different time frames on which the partners operate.

Illustration by Josef Gast

The time from drug discovery to market approval averages about seven years, whether a new compound is the product of genetic engineering or medicinal chemistry. But lacking operating revenues, biotech executives live with the constant need to raise cash, which prompts them to focus on the one-to-two-year windows between financings, and leads to a management style based on snap decisions. With the luxury of positive cash flows, pharmaceutical executives can afford a more deliberate pace.

The big companies "don't understand that we as a company have two years of cash," said Mr. Pops of Alkermes. "Six months to them is not a big deal; six months to us is one fourth of our survival."

From the larger companies' perspective, however, small firms are often in a rush to proceed with marginal projects before they are ready. "It feels to them like we're dragging our feet; it feels to us like they're being naive," said George Milne, president of central research for Pfizer Inc. in New York. "Pfizer's time horizon is 25 years; the smaller company's is probably 5 years and after that it goes blank."

Nevertheless, Mr. Milne said, the biotech industry's time frame is much more in sync with the pharmaceutical companies than it is with the stock market, which lives for quarter to quarter returns on investment. "This raises another important value to collaboration," he said. "What you want is patient money."

The pharmaceutical companies can provide patient money because their investments in biotech still only represent a portion of their overall research and development expenses, which have always been high, and are typically not dilutive of earnings per share. They also understand far better than do public investors that drug discovery is a process that, more often than not, ends in failure.

"Some of the seeds of research are going to get planted by small companies," Mr. Milne said. "But it's going to take the major companies that can devote the scarce resources to convert these to real drugs, and take the body blows that come with 10 failures for each success."



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Biotech and pharmaceutical companies both seek to bring new drugs to market, but beyond that goal their objectives may diverge. Biotech companies typically enter these alliances to insure their short-term survival; they give up a portion of their future upside to have a future at all. Most still intend to proceed as independent companies. The large companies enter these relationships to fill gaps in their research pipelines, to find the new drug candidates that will succeed their current products as they come off patent. Whether the small partner survives as an independent entity is, in many cases, of secondary importance.

"I don't think major pharmaceutical companies have any interest in giving biotech companies the opportunity to become major competitors," said Dr. Vasella of Sandoz. "It is not in your interest to help them become a full-fledged pharmaceutical company because then you lose them as a partner."

Some alliance specialists say that some divergence of goals is inevitable, and that it is simply naive to think both parties must enter a relationship for the same reasons. In that light, the partners can both benefit from an alliance even though their strategic reasons for entering it differ.

"I don't think companies in an alliance should have equal or common goals, but they should have compatible goals," said Benjamin Gomes-Casseres, associate professor of international business at Brandeis University and author of "International Alliances in High Technology" (Harvard University Press, 1995). "We get tied up if we try to think of them as long-term, win-win, and anything else is undesirable. You have to come back to 'we need each other.'"

And "need each other" the biotech and pharmaceutical industries clearly do. There is a timely synergy in the fact that just as the traditional tools of drug discovery are running out of steam, the methods provided by biotechnology are exploding with possibilities. From antisense, which exploits a class of molecules never before considered as drugs, to gene therapy, which harnesses the body's own genetic mechanisms in the treatment of disease, the potential of the new tools is enormous.

To a great extent, these technologies have democratized the process of drug discovery. When discovery consisted of endless screening of proprietary broths of chemical compounds, it belonged exclusively to those companies with the most chemicals. When a small company, using one of the new technologies, can produce compounds never before imagined, drug discovery belongs to the clever and the quick.

But customers--patients, physicians, health maintenance organizations--do not buy discovery, they buy drugs. So there needs to be a level of commerce between the biotech companies with the leading-edge discovery tools, and the pharmaceutical companies with the infrastructure to develop and market finished drugs. The model for that commerce is being worked out in today's strategic alliances.

"I don't think we should strive to be fully integrated, because that doesn't make sense for a big pharmaceutical company anymore either, but that doesn't mean we shouldn't keep a significant portion of our products for ourselves," said Dr. Croke of Isis.

To pursue multiple strategic alliances while remaining independent, a company needs a broad enabling technology, Dr. Croke said. That way, it can partner 50/50 on specific projects, the way Isis has joined with Boehringer Ingelheim International G.m.b.H. on inflammatory diseases, while retaining 100 percent ownership of the core technology. Companies with a single product are better candidates for acquisition than alliances, he said.

"You need a clear vision of the company you want to create, so you recognize what you want to keep and what you want to give away," Dr. Croke said. "You also need a partner that sees it in their interest to have you continue as an independent entity. For that, you need a partner that recognizes we are creating a feeder industry."

Even as the concept of a feeder industry is still being defined, some companies are pushing it to new limits. While a company like Isis still shares in drug development, clinical trials and even manufacturing, a newer group intends to be almost entirely "virtual." These companies believe they add the most value earliest in the drug discovery process, and intend to outsource or partner everything else .



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Perhaps the most extreme are the genomics companies, which are piggybacking on the multinational Human Genome Project to locate and identify every gene in the human body. Most of these companies have no intention of producing drugs, but instead believe that if they can spell out the sequences of genes relevant to specific diseases, they can sell that information for large amounts. From SmithKline Beecham P.L.C.'s \$125 million investment in Human Genome Sciences Inc. of Gaithersburg, Md., which intends to produce partial sequences of all 100,000 genes, to Amgen's payment to Rockefeller University of potentially \$90 million for a single gene believed to be responsible for obesity, the large companies have shown they will pay.



"We don't want to be in the development business; we want to put all the development risk on to a corporate partner," said Kevin J. Kinsella, president of Sequana Therapeutics Inc., a genomics company based in La Jolla, Calif., which has entered strategic alliances with Corange International Ltd., the parent company of Boehringer Mannheim Group; Glaxo P.L.C.; Genentech; and Boehringer Ingelheim.

"The pharma company, like any other, is going to make, on an ongoing basis, make or buy decisions," Mr. Kinsella said. "There is only one gene pool; a big company could spend the next five years creating a Sequana, but they want to be first in the race."

But Mr. Kinsella also said he thinks the era of multiple strategic alliances for genomics companies is a transitional one. "Frankly, I think the exit strategy is, within a couple of years, we'll all be acquired," he said.

Indeed, previous generation biotech companies are already going through that transition. Sandoz, which entered a strategic alliance with Genetic Therapy Inc. in 1991, acquired the company in June. Chiron entered a strategic alliance with Viagene Inc. in November 1993, and acquired the company last April. Chiron itself also agreed to sell a 49.9 percent stake to Ciba-Geigy for \$2.1 billion, after several years of partnering.

As the larger companies identify those technologies that are truly strategic, "many of these alliances end up in a sale," said Peter Pekar, a senior adviser to Booz-Allen about alliances.

It is then that the final benefit of the partnership arrangement kicks in. Compared with an acquisition not preceded by an alliance, "the chances of success go up exponentially," Mr. Pekar said. "You know each other."

New biotechnology companies used to aspire to be the next Amgen Inc., the first fully integrated pharmaceutical company to emerge from the biotech field, thanks largely to two blockbuster drugs. But these days, newcomers are more likely to emulate the Chiron Corporation, which has emerged as a diversified bio-conglomerate. Chiron's ticket to success? A series of canny alliances.

Chiron is still not as large as Amgen, in revenues or earnings, but its strategy is more duplicable, and depends less on luck. And although Chiron is still managed by the three molecular biologists who founded it more than a decade ago, with nary an M.B.A. among them, its success story has broad applications to companies outside biotech.

Since its inception, Chiron has used strategic alliances as a tool to mitigate risk, finance development and broaden its product portfolio.

Chiron has not hesitated to acquire companies when management felt it was important to own an asset, but it has far more often sought partners. Indeed, no other biotech company has partnered as persistently, or been so consistent in negotiating straight 50/50 deals. The result is that Chiron, which is based in Emeryville, Calif., is now a leader on many fronts, including diagnostic tests, vaccines, drugs for a variety of cancers and other diseases and products for eye surgery.

"The degree to which you can tackle diversity with your technology depends upon the degree to which you leverage your technology into other companies' existing programs," said Edward Penhoet, Chiron's president and chief executive.

Chiron sees itself as an organizing force in the assembly of seemingly disparate new technologies that actually complement each other. That strategy requires alliances with other companies, some larger, some smaller, if those technologies are going to lead to new drugs, new diagnostic tests or other medical products.

In many cases, Chiron may not be the company that ultimately sells the drug or test; that depends on the structure of the alliance. "The most important thing a company needs to do is to decide what its product is," Mr. Penhoet said. "The Chiron product equals what Chiron sells, which is not necessarily the same as what the consumer winds up buying."

Chiron holds on to the portion of a product to which it believes it can add the most value. Thus Chiron sells viral-screening technology to its joint venture with Johnson & Johnson, which sells blood tests; it contributes its ability to make genetically engineered mimics of viruses to the Biocine Company, a joint venture with Ciba-Geigy A.G.; and it manufactures Betaseron, a protein-based drug it developed for the treatment of multiple sclerosis, for sale by the Berlex Laboratories division of Schering

A.G. It also sells its own drugs and surgical tools.

>The lesson drawn from these multiple alliances is that a company can engage in many profitable transactions without singlehandedly bearing the development risk, and the infrastructure costs, of delivering a consumer product. Ultimately Chiron succeeds by producing an ever-bigger pie, not by maximizing its own slices.

Chiron's alliances allow it to compete in business segments where it would be hopelessly overmatched on its own in sales and marketing strength, no matter how good its technology. Ortho Diagnostics Inc., Chiron's joint venture with Johnson & Johnson, can go head-to-head with Abbott Laboratories; Chiron alone could not. But Chiron goes a step further: it sells its technology to Abbott as well, which uses it to compete in the blood-screening market against Ortho.

There are still other benefits that come from alliances, Mr. Penhoet said. Collaborating with competitors gives Chiron an opportunity for peer review that is hard to come by in the corporate world, he explained.

"Peer review is an extremely important part of corporate relationships," he said. "One of the most serious diseases that all companies face is isolationism."

Chiron's strategy is not without detractors, and Wall Street analysts long derided the company as diffuse and unfocused and steered investors to competitors with a simpler story.

Even today, some say Chiron's stock price would be far higher if it were not so difficult to quantify the company's multiple business units and partnerships. But investors have nonetheless warmed to Chiron, seeing its expanded alliance with Ciba-Geigy as a validation.

