

COVER STORY



Why do some scientists get such a kick out of their first biotech startup that they can't resist launching a second, a third, or more? Success plays a role, and so does money – but the entrepreneurial urge runs far deeper.

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Aiming For The Next Winner

Unusual as it is to start one successful biotech company, it's even more unusual to start several. Which is why serial entrepreneurs make us wonder all the more: How did they do it? And are there lessons for me?

The lessons are mostly ones you've heard before, no doubt: Get a thorough grounding in science before you start a company; exploit the happy accident; hold fast in hard times; have passion; be lucky. But there are also others mentioned less often, perhaps because some lessons are more easily considered in the experiences of people who have started several companies than in the lives of those who have started only one. For instance, that wisdom may call for letting someone else be CEO of the company you've founded. Or that finding a mentor need not necessarily happen at the outset of an entrepreneurial career.

There are those who believe that being an entrepreneur is something you cannot learn. You either have it in you or you don't. Whether that's true or not, one thing's for certain: Serial biotech entrepreneurs live extraordinary lives.

By Tom Hollon
Special To Signals



"My old pappy used to say that the best way to deal with temptation is to yield to it."

----- Bret Maverick, card shark and riverboat gambler

You have to wonder -- did some of biotech's greatest entrepreneurs absorb pappy's wisdom from actually watching those old 1950s television shows? Or were they just born with pappy's words already pumped into their souls like plasma, destined to surrender to every desire to start a biotech company?

Biotech venture capitalists may credit themselves with originating numerous startups, but more often than not their primary concern is making money, and that is not what we mean here by serial entrepreneurs. No, we're talking about scientists motivated to start multiple companies for different reasons – although becoming wealthy in the process was certainly a plus.

Donny Strosberg will tell you that he's well off, but not the way you might think from all the companies he's started. Friendship has been one of his motivations in addition to science, and startups probably serve as an outlet for his stupendous energy. Chris Henney has always delighted in his companies first for their discoveries and clinical achievements, and only second for their financial rewards. And for Henry Blair, to witness what enzyme-replacement therapy can do, to watch in rapt attention as a bedridden patient literally gets out of bed and walks, has been unforgettably thrilling and motivating. Besides, says the self-taught enzymologist, he hates having a boss. The way around that is to be the boss.



The Night Owl Sidekick

Everyone has a big, big favor to ask Donny Strosberg, founder, president and CEO of [Hybrigenics](#) SA, in Paris, France. "Donny," they all say, "you know so much about starting biotech companies, would you help me start one?"

Since 1984, biotech startups have been all in a day's work for Strosberg, who before starting Hybrigenics was also a highly productive academic researcher with 45 trained PhDs and nearly 400 papers to his credit. All in a night's work,

too: One reason he accomplishes so much is that he goes right on working long after everyone else has collapsed into bed. That's one of his strengths, he says: "Really, I think sleep is a waste of time."

Strosberg, who is Belgian, says he cannot recall the Swiss refugee camp where he was born in 1945. His childhood memories are of Antwerp, where his parents settled soon after World War II. He earned his Ph.D. in protein chemistry at the Free University of Brussels, and returned there in 1973 as a professor after a three-year postdoctoral fellowship at [Massachusetts General Hospital](#) in Boston.



Arthur Donny Strosberg

Strosberg established his two-jobs-a-day routine in 1977 when he became a full professor at the University of Paris while retaining his position in Brussels. Shuttling back and forth between labs went on for three years before he decided Paris was the better place to make his name. In 1985 he made a move to the [Pasteur Institute](#).

By then, however, his career was no longer strictly academic. The year before Strosberg had started his first company, [Chemunex](#) SA, "which develops systems for rapid microbiological analysis in industrial samples," he says. "Later, it was one of the first French biotech companies to be listed on the public market." Chemunex set the pattern he used for startups for the next 13 years. "My way was to put it all together and then remain as an advisor and have other people run it," he says. "I assembled the team, I put together the intellectual property, I helped raise the money and I found a CEO to run it." Hiring CEOs was only common sense, because at the outset of his entrepreneurial career, he explains, "I didn't consider myself ready to run a company."



In the late 1980s Strosberg, recognized as an expert on cell surface receptors, was advising [Genentech](#) Inc. and spending one week each month in the U.S. when he met Moshe Alafi, a San Francisco venture capitalist well known for his investments in [Amgen](#) Inc., [Biogen](#) Inc. and [Cetus](#) Corp. Moshe "asked me to help him with a company that he had started, and then he offered to help me start a daughter company, Ideon, where I could develop my own research and development ideas."

The parent, Invitron Corp, in St. Louis, MO, was a manufacturer-for-hire for biotech companies in need of large-scale production of recombinant proteins. Strosberg located Ideon next to Invitron's research unit in Redwood City, CA and focused his company on therapeutic antibodies and proteins. "Ideon was complementary to Invitron's development of production tools," he says.

Unfortunately, after Invitron's IPO in October 1987 and the company's initial expansion, its business prospects soured. At the time there weren't many therapeutic recombinant proteins to manufacture, and most companies that had developed these proteins preferred to manufacture them themselves. So in the early 1990s, Strosberg folded Invitron's research unit into Ideon and then obtained financing for the renamed entity, [Incyte](#) Pharmaceuticals Inc. (now Incyte Corp.). Not long afterwards, Incyte switched to the business for which it became famous, sequencing the expressed human genome. Strosberg credits the idea to his colleagues from Ideon – the late Jeff Seilhamer and particularly Roy Whitfield, who became Incyte's CEO -- and from Invitron -- Randy Scott, who became Incyte's CSO.



The California adventure did more than deepen Strosberg's business experience. In Alafi he had found a mentor, a friend who over the years has helped him solve many problems. But before starting more companies, Strosberg first had to attend to a problem back home: "The Pasteur Institute didn't like my involvement with the biotech industry."

It was a matter of principle: In those days the administration's view was that scientists at Pasteur did not have ties to industry. "They said I had to choose between continuing my involvement with biotech or my scientific career at the Pasteur," he recalls, "and they were totally convinced that I would stay, because no successful scientist had ever voluntarily left the Pasteur."

Until he did. Although the Pasteur Institute is the top of the line in French medical research, "I valued my scientific freedom and considered that there are other things in life." So in 1990, Strosberg moved his lab together with 50 people into the new [Cochin Institute](#), also in Paris, which he started along with two other scientists.

Startups, now perceived more positively, continued. In 1992 Strosberg helped his daughter Muriel start and run

Vetigen, a company that was "active in allergy tests for animals," he says. "It's still going but she sold off most of the business. Right now the company is more virtual than anything else."

That same year, while he was on sabbatical at [Harvard Medical School](#), Malcolm Gefter at [MIT](#) proposed that he, Strosberg and a third scientist start a company with support and assistance from MIT. The company, Pharmaceutical Peptides, Inc., focused on peptide drugs discovered using phage display technology. Later renamed [Praecis Pharmaceuticals](#) Inc., it is now located in Waltham, MA. Gefter is CEO. "He's the man who really started the company," Strosberg emphasizes. "I was only a sidekick."

"In 1995 I started another company in France at the urging of my long-time associate Pierre-Olivier Couraud, who had also been with me at Ideon, and three of our students who absolutely did not want to go abroad for a postdoc. So I obliged, and that was Neurotech." John Goodhardt, who had run Chemunex for its first seven years, signed on as [Neurotech](#)'s first CEO. Neurotech develops therapies for ophthalmologic and central nervous system diseases.

Where the Fun Is



Increasingly, though, being advisor, teacher and sidekick left Strosberg dissatisfied. "To start a company and then hand it over to somebody else" had become "extremely frustrating," he says. In part this was because too few of his companies rose to the level of his dreams. Incyte and Praecis succeeded, he's glad to say, but in contrast he believes the later management of Chemunex starved the company for capital by treating investors like adversaries. "That's not the right attitude," he warns. "You must have your investors as allies, as your support." Consequently, when the Pasteur Institute came calling with a deal, Strosberg thought the time had come to run a company himself.

"In 1997," he says, "the whole management of the Pasteur came to see me and asked whether I would help them start biotech companies." It was "basically the same group" that seven years before had commanded him to give up his biotech startup activities or leave. Now, "they recognized the need to start biotechs, and since I had a lot of experience, they asked whether I would help them do it."

"You bet I would!" he replied. "Before they had the time to change their minds, I came up with a project and a company and they immediately gave me the space and everything I wanted." Within three months the Strosberg-Pasteur Institute alliance had created Hybrigenics. Strosberg took a leave of absence from the Cochin Institute to become CEO. And following what he taught them, the Pasteur Institute has started about 10 companies, he says.

Hybrigenics sprang from Strosberg's expertise developing screening technologies. Hybrigenics maps protein-protein interactions in order to decipher biological pathways relevant to infectious diseases and cancer. In particular, the mapping technology has been applied to hepatitis C virus and HIV infections. From protein interaction maps Hybrigenics can find, validate and prioritize protein targets for therapeutic intervention. Strosberg anticipates that several anti-cancer drug candidates may soon move into preclinical analysis.

Strosberg admits still finding himself tempted to focus on research instead of development. For example, he says, "If I want to find a therapeutic target to develop a drug, I have to make a selection among the hundreds of protein interactions I've discovered and choose one or two proteins as targets, and then I have to just ignore everything else I've discovered. That's extremely frustrating." But hard choices go with the job, so he makes them and then encourages his team to follow. That isn't always easy: "You have to kill many projects. You have to discourage scientists. You have even to send some scientists back to academia."

Strosberg probably could have started a company like Hybrigenics in the United States. But he stays in Paris for the same reason he turned down offers in the early '90s from [Alza](#) Corp. founder Alex Zaffaroni to start and help run [DNAX](#) and later, [Affymax](#) Inc. -- he thinks France is a wonderful place to live. So he runs Hybrigenics where there are no SBIR grants, fewer venture capitalists, "no public support," science bureaucrats suspicious of industrial biotechnology and severe cutbacks in government support of basic research -- a business climate tailor-made for a man who says he never gives up. "It's easy to start a company in the States," he says. "It's difficult to start one here. Therefore it's more fun to start it here."

"Why Isn't It Good Enough For You?"



Chris Henney knows precisely what motivated him to resign from the [Fred Hutchinson Cancer Research Center](#) in Seattle, WA and turn a downtown office building into the home of one of the great biotech success stories, [Immunex](#) Corp.

Towards the end of 1979, Henney, then chairman of the immunology department, had decided to start Immunex with

Steve Gillis, whom Henney had recruited as an assistant professor. They would run it essentially as a research institute with independent funding -- in Henney's words, "like a mini version of [Scripps Clinic](#)." But should they stay at the Hutch and run Immunex on the side, or jump ship?

Henney hadn't previously considered himself much of a risk taker. While he had risked building his career in America instead of returning to England after finishing his postdoc years earlier, that risk came with a safety net: He knew he could always find a job back home. There was no net underneath Immunex. For someone who "wasn't particularly young and had tenure," was that a gamble he could afford?

Nineteen eighty began with Henney still undecided whether to go or stay, when a recruiting interview suddenly made up his mind. It was "a young woman who ironically never came to Immunex," he says. "She said, 'Oh, yes, this sounds great. New labs, freedom to operate, lots of money. But let me ask you a question: Why isn't it good enough for you?'".



Christopher S. Henney

"Steve and I looked at each other and said, 'That's a totally fair question.' If that was what we were going to hear from the very best people -- which were the kind we were trying to recruit -- well then, let's just do it. If that was the obstacle, we could remove it. And we never looked back."

Still, he observes, "We never really faced the key issue: Could we make it into a business? That came quite later. I think if we had known what it was going to take financially, which was about 400 million bucks, we probably never would have done it."

Feeling they needed a business guide, Henney and Gillis hired non-scientist Steve Duzan to become CEO. One of Duzan's virtues was that, "he knew how to raise money, which we were totally ignorant about," says Henney. They started Immunex "with one million bucks, which in those days we thought was a lot of money."

Cytokines 'R Us

"In the early days we used to call the company Cytokines 'R Us," he says, because Immunex's research program basically expanded the investigations of immune system cytokines he and Gillis initiated at the Hutch. Immunex hired researchers with broader skills than traditional for immunology -- molecular biology in particular -- enabling the kind of "broad brush" research Henney loves, not only broader but also faster and deeper than possible almost anywhere in academia. And by publishing as soon as patent protection allowed, Immunex became a recognized cytokine research powerhouse, which in turn made recruiting talent easier.

But none of this guaranteed profitable products. That required luck. "You see," he explains, "none of us were smart enough to know where the winners were going to come from." He and Gillis initially thought IL-2 would be the winner. "But IL-2 didn't quite pan out. Then we thought colony-stimulating factors were going to be big. Which they were: Through G-CSF and GM-CSF and Epogen (and receptors such as Enbrel), they are the biggest successes in biotech." But GM-CSF (Leukine), which Immunex worked on "for good scientific reasons," was clinically not as good as Amgen's G-CSF (Neupogen).

And Enbrel, "the savior of the company and the reason Immunex is a success," he declares, "was slated at various times to be thrown out." It failed when it was tried against sepsis. Only later did it succeed as a treatment for rheumatoid arthritis. "You never know where your winners are going to come from. Many years and several companies later, I still don't know. So you give yourself as many shots on goal as possible."

As Henney closed in on a decade as Immunex's scientific director, his gratification in seeing Leukine move toward approval coincided with a mounting desire to move on. Immunex was becoming something other than a research institute, and in his eyes, "a little bit less interesting." The reason -- totally normal, he adds -- was the cost of funding commercial development. "By the time I left," he says, "the research budget was about \$35 million a year, yet I felt like I had less freedom to operate than I had with a million."

Viagra, Move Over

ICOS Corp. was born of Henney's enthusiasm for constantly looking for something new: "At the Hutchinson were a bunch of scientists that I had tried to recruit to Immunex." They were investigating the role of immune cell adhesion in inflammation. "The irony was that I could not in an established company get the money together for a whole new

set of activities." So when he decided to start ICOS, he immediately proposed to them an anti-inflammatory R&D program and the kind of freedom to operate that Immunex was losing.

"I had the great fortune of persuading George Rathmann, who had been our competitor at Amgen, to join me. I had heard he was also looking to move on," Henney says. Robert Nowinski, who had founded Seattle-based Genetic Systems Corp. (which was later bought by [Bristol-Myers Squibb](#) Co.) joined as a third co-founder. Their track records made raising \$35 million easy enough for ICOS to employ 65 people on the day it opened in 1989. Henney became scientific director and Rathmann, CEO. (Nowinski left after a year for another startup.)

ICOS' business plan was "to go where the science took us," Henney says. "Our noses, in taking us into good areas, were pretty good, but in terms of absolutely defining what the product was, we didn't have a clue." Indeed, the program that was originally ancillary became the one driving ICOS to its first product. That was the program for which he hired Ken Ferguson, who brought the idea that revolutionized development of phosphodiesterase inhibitors.

Phosphodiesterases had long been drug targets for indications such as hypertension, but the field was littered with failures because of toxicity, particularly in the liver. Biochemists had proven the existence of three phosphodiesterases. Ferguson's idea, to clone the entire phosphodiesterase gene family, revealed over a dozen, with distinct tissue expression patterns.

Henney continues: "I was able to persuade [Glaxo](#) to partner with ICOS in looking for drugs -- conventional drugs, not biotech products -- using our cloned targets." He argued that drug screening using enzymes produced from cloned genes instead of biochemically purified from tissues would yield drugs more specific and selective and therefore less toxic

Ferguson's brainchild resulted in ICOS' first drug, Cialis, which inhibits the same phosphodiesterase as Viagra. Cialis is on sale in Europe for erectile dysfunction and has an approvable letter from the FDA. The anti-inflammatory program continues but hasn't yet produced approved products.

CEO's Nugget

Henney didn't have a mentor in business until ICOS, he says: "Rathmann and I had very much a mentor-student relationship. My years with George were extremely important in confirming that I was ready to be a CEO." In 1995, "George was talking about retirement and I felt I could do the scientific director job standing on my head. I took a job as CEO of Dendreon to satisfy the one thing I hadn't done."

[Dendreon](#) Corp., started by two Henney friends at Palo Alto, CA-based [Stanford University](#) -- Sam Strober, a clinical immunologist, and Ed Engleman, a blood banker -- had two problems. One, it was out of money. And two, says Henney "they really didn't have a business. But the scientific nugget was there." Henney invited David Urdal, his former postdoc who had followed him to Immunex and was still there, to be his partner. Urdal is now Dendreon's president. They recapitalized Dendreon, and then, says Henney, "we totally redid it."

Dendreon had a way to isolate dendritic cells from blood. "That was the part that we seized on," Henney says. With it they created Dendreon's primary R&D program, developing T-cell vaccines for treatment of cancer. He explains that conventional vaccination produces antibodies that are very good against bacteria but not against virally infected or neoplastic cells. "There you need T-cell immunity." Initiating T-cell immunity requires dendritic cells to take up and present antigens to T cells, and until Strober and Engleman discovered how to isolate dendritic cells there was no efficient, reproducible means to do that.

At Dendreon, stimulating strong T-cell tumor immunity begins with the patient donating blood, from which dendritic cells are isolated and then exposed to Dendreon-developed tumor antigens. Two days later, dendritic cells now primed to induce T-cell immunity are returned to the patient by infusion. Dendreon's most advanced therapeutic cancer vaccine is Provenge for prostate cancer, which recently began pivotal phase III testing. Trials for multiple myeloma and breast cancer T-cell vaccines are in earlier stages.

Four years ago Dendreon moved to Seattle and this year Henney stepped down as CEO to become chairman of the board. He passes on to his successor, Mitchell Gold, the lessons he learned at Immunex and ICOS, including the one about multiple shots on goal. For he still hasn't mastered picking winners: "After 25 years, I'm still learning the rules of that game," he says.

The Rebel Who Missed the Boat

Hmm, hot or cold, which would I rather be? Perhaps that's what Henry Blair asked himself when a phone call announced a job opening in the engine room of a [Woods Hole](#) Oceanographic Institution ship about to leave for the

Caribbean. Should he ship out or stay at [Tufts Medical School](#) in Boston, where the job he had just started was shaking a piece of equipment for eight teeth-chattering hours a day in a -20° C freezer?

Blair made a fateful choice, looking back. He will never know what he would have become by putting out to sea. All he knows is what he did become by not leaving the position he'd found through an ad at an employment agency: Co-founder of [Genzyme](#) Corp. and founder and CEO of [Dyax](#) Corp., both in Cambridge, MA.

"I was a rebel," Blair says of his youth. "That's probably one of the reasons I didn't do particularly well in school. I was asked to leave a few of them." But he liked science, which may explain why in the early 1960s the young research technician with only a high school education decided to stay at Tufts and went on to thrive. Blair jokes about being dangerous to be around during the twenty years he spent there as a self-taught enzymologist. But the fact is that he came to be respected -- by the researchers and companies that used his enzymes; by the US Patent and Trademark Office, for his method to measure methotrexate in the blood; and by the NIH, which awarded him more money in contracts than most academic researchers had in grants.



Henry Blair

His time-off activities during those years included his first steps in business. There was his business bleeding horseshoe crabs, with production headquarters an old soapstone sink in the antique house in which he lived. The blood has an enzyme used to detect endotoxin. And there was the tropical fish venture: "I was the first person to ever breed some exotic tropical fish that were brought in from a lake in Africa," he says. "I was very successful at it." If market demand ever picked up from a pair of fish a year, he was ready: He had hundreds.

Far more successful was Enzyme Center, Inc., which in the late 1970s he and his boss founded with the university's permission. They sold enzymes to makers of diagnostic kits. Running the business coincided with his responsibility for large-scale isolation of therapeutic enzymes studied by Tufts researchers.

The Dean's Problem



In his second decade at Tufts fate again altered his path, this time in the person of Roscoe Brady of the NIH. "Brady was very well known in the area of metabolic diseases, particularly lysosomal storage disorders," Blair remembers. "He was the first to identify the defect in Gaucher disease." The disease traces to a recessive mutation in the glucocerebrosidase gene. Its effects on infants are horrible -- not only ataxia, seizures, and dementia, but also bone lesions, hematologic abnormalities and enlargement of the spleen and liver. Blair worked with Brady on Gaucher and Fabry diseases for seven years, frequently working in Brady's lab. "He was a mentor to me," Blair says fondly. "I learned an enormous amount from him."

As a result of that experience, Blair received a 3-year NIH contract to build and operate at Tufts a larger facility for producing glucocerebrosidase for experimental therapy. And that led to conflict with university administration. "The dean of the medical school really wasn't quite sure what to do with me," Blair explains, "because I was a non-professor and I had an enormous amount of funding." Maybe the dean would have been more sympathetic if he had been a Ph.D. or M.D., he says, but in any event, the dean refused to provide any space for expansion.

Blair responded by looking for a way around the dean -- and opened doors he didn't realize existed. "I had never heard of a venture capitalist up to that point," he says. But soon he was in contact with one, who introduced him to entrepreneur Sheridan Snyder, and together they solved Blair's problem. "We could not move the contract," Blair says, "but we could subcontract it." And that's what they did -- subcontract to Genzyme, the company Blair and Snyder founded in June 1981. Three years later, when the contract was up for renewal, Genzyme took it over completely. Today Genzyme employs 6,000 people.

"Sherry was president. I was vice-president and ran most of the company," Blair says. Snyder knew almost nothing about the business, but Blair credits his partner for teaching him an enormous amount about being an entrepreneur. He remembers Snyder as well for pulling out all the stops as a salesman: "We'd go to meetings and I would shudder at what he would promise, because I was the one who had to deliver it. He had no idea what he was offering. But it was a lot of fun."

Genzyme's initial capital was their own money and a British bank loan. Venture capital didn't come in until after the first nine months. And getting it wasn't easy: "I remember speaking to venture capitalists and watching their eyes roll into the back of their heads when I told them I was going after a disease with 1,000 to 10,000 patients," Blair says. "That drug now sells on the order of \$700 million a year. But they didn't quite see it back then."

The Razor Blade Adventure



In the fall of 1983, their partnership came to a halt: Henri Termeer was brought on board to replace Snyder as president. "Henri had the vision to see that the Gaucher product was actually viable," says Blair. "He did well in raising the money to do the pivotal trials, all \$10 million of it for all 12 patients. Fortunately, it worked in all 12. That was probably the smallest clinical trial that has ever been run." Under Termeer, Ceredase (glucocerebrosidase purified from human placentas) received orphan drug status in 1986 and marketing approval in 1991. Cerezyme (recombinant glucocerebrosidase) was approved in 1994.

Snyder left Genzyme soon after Termeer came in. As for Blair, "I stayed around for a while with Henri, and I have the greatest respect for him, but I've never worked very well with a boss. Sherry and I were equals and did different things. Even at the university, the person who ostensibly was my boss was off doing something else. It had been many years since I'd had a boss, and Henri and I viewed some things differently." Blair stayed on the board after his exit from Genzyme, but otherwise did little, going "from having five people standing outside my office at any one time to an office on Cape Cod, staring at the phone in the consulting business, waiting for it to ring."

His fallow period lasted but a few months, ending the day he heard of an opportunity to acquire a unique chromatography particle developed by Alcoa. "Sherry wasn't doing anything and I wasn't doing a lot," Blair remembers, "so we pulled ourselves out of retirement." In 1989 they raised venture capital and started Biotage Inc., intending to use the particle as their entrée into purifying biotherapeutics.

The revived partnership was eager not to waste a moment: "The Alcoa people said their technology needed 'a little more work,'" Blair recalls, "so in the meantime we were preparing, because this was going to be great." Blair and Snyder went shopping, gathering the technology to exploit the particle by purchasing two large-scale chromatography companies and a small outfit that purified antibodies. Getting the particle ready to exploit, however, was taking longer than expected. Months of tinkering at Alcoa stretched into a year, and then two, until at length the Alcoa people offered a revised assessment of the particle: Perhaps effervescent proclamations of its extraordinary chromatography capabilities had been somewhat premature.

"That's an understatement," Blair growls. "It didn't work at all. After two or three years we ended up with a really terrific razor company and no razor blade."

"Unbelievable"



Though wounded by the particle fiasco, Biotage did not go under -- in fact, it eventually healed very nicely -- thanks to an employee's idea to sell ready-to-use chromatography media packaged in disposable cartridges. The company made the adjustments necessary for survival and Blair, meanwhile, kept his eyes open for a way to get Biotage into the pharmaceutical business.

Within a couple of years he found what he was looking for in a small company called Protein Engineering Corp., a pioneer in phage display technology. "Back then no one had ever heard of phage display," Blair says, "which is an excellent way to discover peptides that will bind very tightly and specifically to a target." Blair thought phage display had great potential for affinity chromatography for pharmaceutical separations -- if only the partner he was trying to woo would be interested. "For years I talked to them about licensing it for that application but they were going to conquer the world and I couldn't get their attention."

Protein Engineering only came round when there was little alternative: In 1995, its money was running out. But instead of talking about licensing, Blair boldly proposed a 50-50 merger with Biotage. He found selling the idea to both boards and finding an investor relatively easy. What followed -- "the most complex transaction I have ever done: a recap of two companies and a merger and a financing all at once" -- was not.

The negotiations that created Dyax "were unbelievable," he declares. "Every time somebody pushed in one place, it would pop out in ten others and we had to get it all back in the box." On the day the deal closed, Blair remembers walking into a very large conference room, "with probably 40 different documents all the way across the table. Then someone pushed it one last time and I went to my attorney and said, 'You know, I'm not going to do this.' He calmed me down and then I signed them all."

Gratification



Since the merger, phage display technology has proven its ability to create drug candidates worthy of clinical trials. And while Blair's idea to combine phage display with affinity chromatography is being accepted for research reagent separations, there hasn't been similar success with pharmaceuticals. "The production end of the biopharmaceutical industry is extraordinarily conservative," he says.

Biotage and Dyax didn't take up all of his time in the 1990s, as occasionally he accepted other business opportunities. He co-founded [GelTex Pharmaceuticals](#) Inc. when someone approached him with an idea for a new polymer technology. GelTex was ultimately sold to Genzyme. It "came up with a good product -- entirely different from what we started the company on, by the way," he says. Later, he took over a small British company called [Biocode](#) Ltd. after hearing that Shell Oil wanted to sell it. Biocode is in the brand protection business. By mixing marker chemicals into fuels, drugs and other products, Biocode can prove the products are genuine rather than counterfeit or adulterated. Biocode detects the marker chemicals using immunoassays. Blair has since stepped off the board, but notes that Biocode is profitable.

In the last two years he has focused Dyax on pharmaceuticals, funding the hiring of clinical, manufacturing and regulatory specialists in part with the profits of Biotage's disposable chromatography business. Phage display technology identified Dyax's most advanced drug candidate DX-88, a potent peptide inhibitor of plasma kallikrein, which is now in Phase II trials. Kallikrein plays a role in regulating inflammation and blood clotting. The indication is hereditary angioedema (HAE), one of those rare disorders that causes sufferers to go from doctor to doctor for years before finally getting diagnosed.

An autosomal dominant genetic disease estimated to occur in 1 in 10,000-50,000 people, HAE manifests in acute, episodic swelling of body parts, usually the face, abdomen, hands and feet. Abdominal attacks are severely painful. Attacks that narrow air passages can kill. DX-88 replaces C1 protease inhibitor, the kallikrein inhibitor present in HAE sufferers in abnormally low levels. A second indication for DX-88, currently in a Phase I/II trial, is reducing blood loss during coronary artery bypass surgery (CABG). The potential American market is 600,000 patients a year.

"People don't realize how big a market an orphan indication can have," Blair says. "There are a lot more HAE patients out there than anyone realizes." He illustrates by describing a recent breakfast Dyax sponsored for an HAE society: "The breakfast was set up for 80 and I expected five to 10 patients to show up. It was standing room only -- all patients." How warm it made him feel when patients came by to greet him and speak words of thanks. It was not unlike his treasured memory of joining Brady at NIH to be on hand for the first Gaucher disease patient treated with glucocerebrosidase. The little boy "had an enormously enlarged spleen and liver. Very, very little energy. He went on to be on the Duke track team and got married a couple of years ago. That's a very gratifying feeling," Blair says.

And to think how different it all might have been if, so many years ago, he had chosen the engine room and the Caribbean over his lowly beginnings in a freezer at Tufts Medical School. Blair pauses a moment.

"I damned near took it."

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