Howard Greene

Interview conducted by

Matthew Shindell, Historian

October 8, 2008

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Howard Greene

Mr. Howard E. Greene, Ted Jr. served as the Chief Executive Officer of Amylin Pharmaceuticals Inc. from September 1987 to July 1996. Mr. Greene Co-founded Amylin Pharmaceuticals Inc. in 1987. Mr. Greene Co founded Biovest Partners. Mr. Greene was a full-time employee at Amylin Pharmaceuticals Inc., from September 1989 to September 1996, and a part-time employee and Chairman of the Executive Committee until March 1998. Mr. Greene was founder and served as President of Epimmune Inc. from July 1987 to January 1989. Mr. Greene served as Chief Executive Officer of Hybritech Inc. from March 1979 until its acquisition by Eli Lilly & Co. in March 1986, and was co-inventor of Hybritech's patented monoclonal antibody assay technology. Prior to joining Hybritech, he served as an Executive with the medical diagnostics division of Baxter Healthcare Corp. from 1974 to 1979 and as Consultant with McKinsey & Company from 1967 to 1974. He was General Partner of Biovest Partners from October 1986 to July 1993. Mr. Greene is an Entrepreneur who has participated in the founding and/or management of eleven medical technology companies over a 22 year. He serves as Chairman of the Board of Directors of Cytel and Satiogen Pharmaceuticals, Inc. Mr. Greene served as Chairman of Epimmune Inc. since January 1989. He served as Chairman of Amylin Pharmaceuticals Inc. from 1987 to 1998. He serves as Director of Tandem Diabetes Care, Inc. He has been Director of Biosite Incorporated (Formerly Known as Biosite Diagnostics Inc.) since June 1989. He serves as a Director of CoDa Therapeutics, Inc. He serves as a Director of Allergan Inc., and a Trustee of the Scripps Clinic and Research Foundation. He served as a Director of International Biotechnology Trust PLC until December 18, 2001. He served as Independent Director of Amylin Pharmaceuticals Inc. from September 1987 to April 7, 2009. He served as a Director of Neurex Corporation since November 1986. He is an accomplished entrepreneur and investor in the biotechnology industry. During a business career spanning over three decades, Mr. Greene has gained experience in various aspects of early stage medical technology companies. Both as an inventor and entrepreneur, and as a venture capitalist, he is

involved in starting, funding, and/or managing ten technology-driven enterprises, all of which have gone public. Mr. Greene holds several patents directed to using the hormone amylin in diabetes therapy. He received a B.A. in physics from Amherst College and an M.B.A. from Harvard University

Source: Bloomberg Businessweek

THE SAN DIEGO TECHNOLOGY ARCHIVE

INTERVIEWEE: **Howard (Ted) Greene**

INTERVIEWER: **Matthew Shindell, Historian**

DATE: **October 8, 2008**

SHINDELL: Right now.

GREENE: Okay. Four score and seven years ago our forefathers brought forth on this continent a new nation conceived in liberty and dedicated to the proposition that all men are created equal.

SHINDELL: Looks like you're picking up just fine then. Okay.

GREENE: Okay.

SHINDELL: So, it's October 8, 2008. This is an interview with Howard "Ted" Greene. Interviewer is Mathew Shindell. So, if you could please tell us, starting off, how did you get involved in San Diego biotech?

GREENE: All right. Well, it started with getting involved in California. I worked for a company called Baxter, which still exists as Baxter International, and I was transferred to their Costa Mesa division. I worked there for a couple of years in a marketing role in a diagnostic division, which was working with antibodies. In that case it was conventional anti-serum from animals. And, I got fired. It wasn't that I was incompetent, or lazy, or anything. I just didn't fit in a large company. And so, Baxter said, "Look, you take all the time you need and help us with some strategic things, but go find yourself another job." At the time, the monoclonal antibodies had emerged as an academic curiosity and I had attended a conference sometime earlier where they were presented. At the same time that I was being let go the decision was made to move the division back to Chicago. And so, a group of other employees, scientists, marketing people, and whatnot, in addition to myself, had decided we didn't want to go back there so we set about starting a company to produce monoclonal antibodies. We hooked up with a professor at UC Irvine, whose name

happens to be Jim Watson. It's not of Watson and Crick. And anyway, we rented a lab space next to where the division of Baxter was located, started buying equipment from Baxter, because they were closing down their labs, and I set out looking for money. I made presentations to several companies, Beckman in the local area. Centex in the Bay Area. And I was, just to hedge my bet, kind of paying attention to potential jobs, because, startups are iffy things. Anyway, our startup company was called Cytex and our first goal was to raise some money so that we could actually function. Meanwhile, I got a call from a headhunter who was looking for a marketing position for a new startup company called Genentech. And, when he described what they were trying to do in the gene splicing area my reaction was, "Aha! They're into so-called genetic engineering," (I don't think the term had even been invented yet) "and maybe I can learn something from them, or maybe I want the job." So, I went up to San Francisco and spent a day with Bob Swanson, who was the founder and CEO. With his gang I got along great, and I told Bob I really wanted to start my own company. It wasn't competitive. He called me that night and said, "You know, you'd be great for my marketing job, but even better for something my partner Brook Byers is working on. He wants to start a company to make monoclonal antibodies." Uh oh. I didn't let on that that's what I wanted to do, but you know, because my partners and I had agreed we ought to keep it confidential. The next day Brook called. He was the junior partner at Kleiner Perkins, and informed me that he was starting a company in San Diego, called Hybritech. In fact, I think they had just, the week that we got together was the week that they had just put $300,000 into it to rent lab space and hire a couple of scientists. , It was started by an academic, Ivor Royston, and I had the industrial experience. So, Brook said, "Let's get together. We'll talk about this thing." And so, we met at Oceanside. We spent a couple of hours. By then I knew a lot about monoclonals and it was pretty clear to him at the end of the meeting that I was already well along in thinking about it. He finally managed to get out me that, "Yeah, I'm trying to start a monoclonal company." And so, we decided, "Well, all right. Let's have a summit meeting." We both agreed that there was not room for two companies. So, we met at my apartment in Newport Beach. It was on Balboa Island. Tom Perkins came down. Perkins, at that time, was basically in charge. And, we talked it all over. Well then they started actively trying to recruit me. By then Cytex had gotten interest from Syntex in doing some funding, but it was still very early stage, and basically there were some stresses and strains starting to develop within my team as to who was going to be in charge, and this, and that, and so on. So, Perkins invited me to come up to San Francisco and sit and talk with him about it. I'll never forget. At one

point he said, "You know, if you start the company in, in Orange County I'm sure it'll be a success, because you, you appear to me to be a good guy. But," he says, "if you do it with us," he says, "we know how to build big companies. We can help you build quickly. You will be famous. You will be quoted in Business Week." Fast forward. Six months later I was quoted in Business Week. I didn't realize it, but at the time they were discussing, you know, a story with Business Week. Well, I was pretty impressed. Tom is one of the smartest guys I've ever known. Certainly one of the best venture capitalists that has ever been in the industry, and after talking it over with my brand new wife – I was actually fired the day I got back from my honeymoon - we decided, "Okay, that makes a lot of sense," and so I decided to join the effort and started driving south. By then they had set up labs. It turned out also San Diego was a better place. Back then there was no Internet. There were really only two medical libraries of any significance in the whole UC system. One was San Francisco and the other was San Diego. And so, basically San Diego represented a strong academic base and at that point that was really all we could draw from. We were hiring junior scientists right out of academia. Anyway, I think if you put timelines on it, my pink slip arrived in early July of 78, I met Brook in probably October of '78, which is, I think that's the official founding of Hybritech. In fact, we just had our, our thirtieth anniversary.

SHINDELL: Oh, I heard you guys had a party over there.

GREENE: Yeah. By March '78 I was still an employee after eight months, nine months, after my pink slip and I formally resigned from Baxter and started commuting down here. Anyway, that's how I, sort of circuitous as it was, got involved in biotech down here.

SHINDELL: Can I ask you, how did monoclonals sort of cross your radar?

GREENE: I'd gone to a conference. Again, I was operating in the diagnostic business and antibodies were an important reagent that was used in a variety of tests, pregnancy tests, serology tests, things like that. And, one of the speakers was Bill Dryer, who at the time was at Caltech and may still be. And, he got up in front of this conference. It would have been, about '76 or '77 is when I went to this conference and Bill Dryer got up in front of us all and he says, "Look, I have a speech that was prepared to talk about fluorescent tagging of antibodies," meaning antiserum, "but," he says, "I'm going to drop that subject because," he said, "the greatest breakthrough in the history of, of, you know, antibody technology has just been made in England.

It's called 'monoclonal antibodies.'" And, he proceeded to make his own predictions about how this was going to absolutely revolutionize the use of antibodies in all sorts of medical products. And, at the time I was pretty darn impressed. In fact for years after at Hybritech we used to invite Bill to stop by on his way to his Mexican cottage. And, we referred to him as Buck Rogers because Bill's mind was always five years ahead. He foresaw genetic engineering of monoclonals at least five years before the first successful attempts were made. And, so that planted it firmly in my mind. When notice came from Baxter that I was a short-timerin conversations with one of our scientists, it turned out he was interested in monoclonals also and knew Jim Watson at UCI. We went to Watson's lab, and he showed us how he did it, which was not very complicated. In other words, it didn't require spaced age, sophisticated laboratory, just a protein chemistry or a cell biology lab. So, by the time he was through demonstrating it I figured, "Hey, we can do that," so, we went down to the UCI cafeteria or whatever it is and ordered a pitcher of beer, and by the second or third pitcher of beer we had all decided, "Let's start a company." So, you know, that's basically how it came about.

SHINDELL: Now, that you were interested in monoclonals and that Ivor Royston and Howard Birndorf were also sort of trying to start up their company, is that just sort of incredible serendipity or, were there . . .

GREENE: No. No. It was time. There were companies starting, and it turned out there was another company starting in Philadelphia.

SHINDELL: Oh, okay. Because one thing I wonder is how aware people were of monoclonals and how, how many people roughly sort of had an idea that this was going to be a big breakthrough?

GREENE: Most of the knowledge was in academia. Okay? I mean it was, it was a hot, hot thing in academia. Ivor got into it because his field is cancer, particularly blood cancers. And he, along with a number of other people realized that one of the things you could do by cloning antibodies this way was to raise antibodies to antigens which are proteins on the surface of cells that would be impossible to do by trying to isolate these proteins and inject them into animals to stimulate an immune response. Instead, what you did is you just immunized a mouse with the whole protein gammish that had all of these antibody targets and then by separating the antibodies out you could, it wasn't easy, go through and you could find those antibodies that

related to certain cells that correlated to cancer. And, that's what Ivor was doing. Have you interviewed Ivor, because he can . . .

SHINDELL: He's actually next on the list.

GREENE: Okay.

SHINDELL: I'm doing him next week. I did Howard. He was the first, the first interview.

GREENE: Okay. Well, the way I understood it was Ivor mentioned to his wife Collette that there might be an opportunity to start a business, because Ivor's one heck of an entrepreneur. And Collette said, "Well, you know, I used to date this guy, Brook Byers, and I think he has something to do with venture capital." And so Brook had come down and Brook had Ivor write him a letter explaining what he proposed to do. And, in fact, that letter is part one of the Hybritech case at Stanford Business School. So, if you track that down you get the historical document. The case was put together by Pitch Johnson, who was one of the early Hybritech investors, very early, and he was teaching the entrepreneurial course at Stanford. And, part one was Ivor's letter where Ivor essentially wrote that using hybridomas we would be able to mass produce antibodies, highly-pure antibodies, which would reduce the cost. You wouldn't have to have, you know, herds of animals, or mice, or rabbits, or whatever. And so, we could sell these antibodies cheaper and we could capture the market for antibodies, which at that time was probably a couple million dollars worldwide. The second case is the business plan I wrote, which started as the Cytel business plan. Within six months of joining Hybritech we were making good enough progress that Kleiner Perkins said, "All right. You've got to raise more money." So, I refined the business plan and used that to raise our first real round after the seed round. The seed capital of $300,000, was basically proof of principle. And here's what happened, as I understand it (I wasn't there) I'm told that it was worked out at the airport where basically Tom and Brook had come down here to go through the lab with Ivor and Tom said, "Look, here's what we'll do. We'll give you $300,000 for sixty percent of the company. You take the $300,000 and if by the time you've mostly run out of it there's something here, we'll go from there. If not? Well, no hard feelings. But, it looks like an interesting project for us." Which, I think is reflective of the way venture capital used to be done. There was no massive business plan. It was just sort of, "Well, let's seed this thing with a little bit of money, see if these guys can actually start to put

something together that will, looks like it's leading somewhere. And if they do we'll go raise real money. And, if they don't, eh, $300,000." After all those guys probably spent more than that on their annual rent since they were in downtown San Francisco. So, by the time I came aboard they were about the two hundred, of the $300,000 left. I was paying myself $40,000, which was a big cut in pay from Baxter. So there went a good chunk of it. So, I updated my original business plan. My business plan was very different than Ivor's, and I think this is what intrigued Tom. I was promoting the notion that these antibodies would make it feasible to produce much more useful products. In other words, products that could not be made with conventional antiserum that now could be made with, with these monoclonals. Better diagnostics, therapeutics, and basically my business plan was to put together proprietary products and charge a premium for them. And, I think that intrigued Perkins and Byers. At Stanford, we'd go through this two-part case and Ivor would come up for the first day to give all the background (and I'll let him, corroborate my memory), and then I'd come up the next day and at that point it was a sort of a big investment decision, all of the $ 1,600,000 million was what we raised. Back then that was, enormous! And, the students would go through the whole thing. But for me the, the real lesson from it was that my business plan focused on, on inventing novel new products and charging a premium for them which was more attractive in the medical field than, than selling antibodies at a discount.

SHINDELL: Right, because the original business plan was basically saying that they had found a cheaper way of producing more pure ones?

GREENE: Yeah. And, I wouldn't take my word for it. I'd get those two – because they're in the Stanford Library of Case Studies. Just go to the database and say, "Hybritech," and there's Part A and Part B, and all, all Pitch did was copy Ivor's letter and my plan.

SHINDELL: I'd like to talk a little bit about your background. You did your undergraduate in science at Amherst in physics, right? And then you went on to get a business degree at Harvard?

GREENE: Right.

SHINDELL: And . . .

GREENE: And at Harvard I specialized in decisions under uncertainty, which was Monte Carlo and that kind of thing, which was a kind of a natural extension of the physics math. And, I've always had a fondness for that.

SHINDELL: So, your business degree was pretty connected to it?

GREENE: It was more toward the technical side, yeah.

SHINDELL: Oh, okay.

GREENE: But, it was at Harvard which is the liberal arts school of business education.

SHINDELL: Oh really? Okay.

GREENE: I came out of Harvard. I was fortunate to be a Baker Scholar, which is the top five percent or something, so I got lots of job offers. In fact I think I made trips to twenty-one different companies. Just dumb. I didn't know what the heck I wanted to do. And, I got an offer from McKinsey and Company, which struck me as a pretty, pretty classy outfit, and they would put me in the Chicago office so I could send the family to Michigan for summers. And, I decided that was a way to take a job without making any decisions about what I wanted to do. So, I was with McKinsey for seven years. In fact, I basically was a pioneer at McKinsey in using computer modeling for, business plans and that kind of thing. And, I was using GE Timesharing at the time, because there was no, you know, PC, or anything like that. Anyway, one of my clients was Baxter. At the time Baxter's CEO was a man named Bill Graham, who to this day I think is the most accomplished, tremendous CEO I've ever known or worked with. And, he had a very interesting philosophy in management and that was he simply hired the best and the brightest and the most ambitious people that he could hire and then created something for them to do. He didn't have a sort of a list of job openings. And, in fact, a professor at Harvard, Monica Higgins, has written a wonderful analysis of the Baxter management style. It's called Career Imprints. She basically was trying to answer the question of why Baxter alumni were so overrepresented among the biotech CEOs. She has data showing that when you compare Baxter, based on its size, to Merck, and Abbott, and some of the others, J&J, that Baxter was the prime source of biotech CEOs. I think for me the combination of McKinsey and Baxter was great. McKinsey was an extremely analytically-oriented environment where I ended up doing a lot of strategic planning, very analytical

planning. I was trained thoroughly in communications skills, because in the consulting business, you know, maybe half the job is to figure out what the client should do, but the other half of the job is to convince them to do it. And so, they have to this day a tremendous editing capability and all, there is just no better training in how to communicate than McKenzie, or BCG or whatever. This served me extremely well when it came time to go out and start pitching Hybritech's business plan, going to Wall Street and so on. I was ready. The other thing, of course, was Baxter's management style, namely this philosophy of bringing really, really bright people in and pushing responsibility onto them way sooner than their age and career experience would, would suggest. And the good ones rose to the occasion. Higgins' book is full of anecdotes. It focuses on Gabe Schmergel, who was made the general manager of Germany, I think, at the age of 29 or something like that. But, that was Bill's philosophy. And, I carried that philosophy to Hybritech. We just had this reunion and, and you know, everybody's talking about, a lot of the people there said, you know, "Never again have they ever worked for a company that was as much fun as Hybritech." And, I really think it was that management philosophy of, you know, hire the best and the brightest and give them responsibility that was what made us so successful.

SHINDELL: So, would you say a few things, about the day-to-day work at Hybritech? Like, what was it that made that work environment fun and productive?

GREENE: Well, number one, we were on the cutting edge of science, and I don't think you would have had nearly as much fun at Hybritech if you weren't just totally enamored with the science and what it could do in the field of medicine. And, that was the, that was sort of the spiritual glue that held us together. . We used to have Friday, TGIFs. It started usually about four or four thirty. They began when I would duck out and go get a six pack. Pretty soon I was having to buy a case, so we decided to institutionalize it and we would bring a keg in. And, it was a great get-together because everybody had been working like mad all week and it was an opportunity to informally kind of catch up with each other. "What happened to that experiment you were doing?" "Oh boy, I just saw something in the literature about this and I'm going to," you know, whatever. And, at those TGIFs everybody talked science. Not baseball. We weren't talking about vacations we'd just taken, or anything like that. It was all focused on the science. So, to my mind, and I think that was characteristic of Genentech. They were equally fanatical about what they were doing. So the point was when you believed so thoroughly in what your science could do you were willing to

undertake things that the rest of the world knew were impossible. And, the big companies, I mean the large companies, were basically ignoring the field. I found out afterward when I made my presentation to Beckman about Cytex I got no response from them. They never even had the courtesy to call me back. But years later I found out that they'd just had Cesar Milstein, who's one of the co-inventors of monoclonals, come through and give a seminar, and they decided to set up a hybridoma lab. I learned this probably, oh, five years later and at that point I decided that they had probably the earliest and least productive hybridoma lab in industry. Because, it went nowhere.

SHINDELL: Why do you think that they weren't able to, to take that forward?

GREENE: Because they're, they are like all big companies, they are a big structure and they formalize budgets, and they hand out money and project goals, and the employees are relatively risk-averse. You don't get ahead in a large company by making mistakes or having projects fail, and, and I just think innovation is hard in that kind of environment – I mean, I'm not picking on Beckman, per se. It's common with all the big companies and it's why every new area of technology inevitably is dominated by startups. The only company I know that has really sort of started a whole industry over and over again is 3M. And, they clearly have a rather unique management philosophy thereof, letting people do entrepreneurial things within the context of the overall company. But, folks like Beckman were very good at what they did because they had strict control over what they were doing. That was the key to their business. And what is the key to making the best voltmeters in the field is not conducive to the kind of wild and crazy innovation that we were doing.

SHINDELL: Would the sort of corollary to that be that a conservative startup company just wouldn't work? You have to be sort of risk averse to be a good startup company?

GREENE: I think so. Look, first of all I would say luck plays a serious role in these things being at the right place at the right time. Of course, some people take advantage of their luck. Others let it go right past them. But, I've felt, and I've not done a thorough analysis of this, but I've always thought that the startups in the biotech field that have been the most successful have been from the top down, starting at the CEO, science-driven. And one of the mistakes that I think a lot of venture capital firms have made is when they get one of these enterprises started they

go out looking for the accomplished executive, whether he's a marketing guy, a manufacturing guy, a research guy, whatever, and bring him in. And, my guess is that if you did a study of, you know, skill sets at the top as a function of relative rates of success that you would find that the best companies, most successful ones, were driven by the science at the very top. Bob Swanson was a science nut. Okay? Ted Greene, a science nut. George Rathmann, who was the founding CEO of Amgen, he's a PhD. He's a real scientist, okay? Mike Reardon, who started Gilead. I mean, these people who have an understanding of the business and inherent leadership skills are driven by the science. I would, I sit in science meetings and I asked all kinds of questions. And, I remember the day I left Hybritech. One of the senior scientists came into me in tears, and said how sorry the scientific group was to see me go, because I really understood what they were doing.

SHINDELL: And, do you think that's rare in CEOs? . . .

GREENE: Yeah, I think it is.

SHINDELL: Yeah?

GREENE: I think it is. There have been exceptions, because, this is not an exclusive thing, and as I say it's more the odds of success than it is whether somebody's going to be successful. But, yeah, I think if you went across the industry you'd find that most of the so-called managers that have been recruited into the business are business managers. They're successful executives. They've risen to the top at J&J, or at Merck, or, you know, Abbott, or Baxter, or whatever it is, and their skill set lies primarily in the sort of management area. Some of them are great leaders and when you're starting a little tiny company management is not what the company needs. It needs leadership. It needs vision, you know. It's not very complicated. In fact, things change so fast that you try to lay out an annual budget and within three months you're making all kinds of changes.

SHINDELL: It seems like this would be an easy thing to explain to a venture capital firm? But I get the impression it's not?

GREENE: Well everybody knows I'm not very fond of the venture capital industry as it exists today.

SHINDELL: Well, let me ask you about that then, because you mentioned earlier that when Hybritech was funded it was funded the way that venture capital used to work?

GREENE: Used to be done.

SHINDELL: Right. So, so what has changed and why, why are you no longer a fan?

GREENE: I'll give you an example of how it used to be done. One of the people I got to know real well was Benno Schmidt. Now, Benno claims to have – claimed, he's now died -- to have invented the term "venture capital." He was the managing director of J.H. Whitney, which was the first firm that was actually doing these kind of startup investments. There was nothing at the time that specialized in that sort of thing. And, at one point they were printing business cards, he said, and they had to come up with some description of what J.H. Whitney was all about, and so he figured that "venture capital" described it well. Anyway, Benno told me a story that I think illustrates the way that VC was done back in the '70s. He said he'd started to get word that a very bright young man from Hewlett Packard, named Tom Perkins, was starting a venture capital firm in San Francisco. So, he called Tom up and said, "Look, next time you're in New York stop by and let's get acquainted." So, Tom did. And, after I suppose they had lunch together or something like that, Benno said, he said to Tom, "Look, I'm working out here on the East Coast. You're working on the West Coast. How about when I get something interesting here I'll give you a call to see if you want to participate and vice versa?" So, time goes by and Benno's on a business trip to Japan and Tom calls J.H. Whitney to speak to Benno. He gets shunted to a junior, partner, explains that he has this deal, a company called Tandem Computers, (which turned out to be one of the all-time big hits of the late '70s), and he thought maybe Benno would like to participate. And, so the junior associate said, "Fine. Send us a business plan and we'll be back to you in thirty days." I've heard this story from Benno probably three times and at that point every single time Benno got tears in his eyes, because he says, "You know, I never got a call back from Tom Perkins ever again." And, basically what that reflected was the way business was done between Perkins and Art Rock and Pitch Johnson, and so on. They would each start to sponsor their own little startup. Another anecdote. This case study that Pitch taught at Stanford. One time I was there and he was going through discounted cash flows. He had my financial projections and he was trying to show the class how you do an internal rate of return and figure out whether it looks like a good investment at whatever value. And, when he got done with it I said, "Pitch, can I ask a question?" He said, "Sure."

This is in front of the class. And I said, "You were a real early investor in Hybritech, weren't you?" And he says, "Yup." And I said, "Well, why did you invest?" And he said, "Well, Brook called me up and said it was a good idea." And he suddenly realized what he'd just said and he went, "Ha!" Because he'd just completely undone all of his rigmarole about, you know, return on investment. And, I think what's, what's happened and one of the sad things about venture capital now is that it is so institutionalized that that's what they do: they work their spreadsheets and they work out their IRRs and all this kind of stuff, and their deal structures have become so complicated that even they don't really understand them, and it's just a very different thing.

SHINDELL: So, there's no intuition, no sort of human element to it?

GREENE: Well, the intuition is primarily related to who you're investing in. Because, you know, frequently brilliant people see things that others can't. Whether at the time Tom Perkins really could comprehend, you know, where monoclonal antibodies could go, I don't know. We tried real hard to lay it out as clearly as possible and I think certainly in our ultimate business plan it was pretty well done. But to this day, I think Tom was much more concerned about was whether to bet on me. And on team I built. And by the way every single senior manager and leader I hired flew through San Francisco to sit and talk to Tom so Tom could give him this speech about, "We build big companies." I think without Tom's help we would have never been able to attract the kind of people we did.

SHINDELL: Let's talk about that for a minute, because when you first came to Hybritech there obviously wasn't a biotech cluster here in San Diego.

GREENE: No, there wasn't. There wasn't even a term "biotech."

SHINDELL: Right. But by the time you left Hybritech there was already a cluster forming here and since then it's become one of the densest clusters in the country in terms of biotech?

GREENE: Certainly relative. The thing that I would love to see is some sort of a measure of biotech's importance relative to the other high-tech industries here in San Diego. In the Bay Area there are, there's probably more employees, engaged in biotechnology but relatively speaking it's less important. Because, they have the

whole Silicon Valley, you know, whether it's the hardware or software, or whatever. But here in San Diego, biotech's a big deal.

SHINDELL: So, how do you think that happened? How do you think it became a big deal here?

GREENE: Well, there are a number of ways. First of all, Hybritech was a great role model. And, I remember when we first started we tried to rent everything because we didn't want to buy anything. And, real estate was something we needed. We needed wet labs, which at the time cost over $100 a square foot, when most of the developers were looking at maybe $15 a square foot. So, when we got ready to build our first plant to make product we couldn't find any local developers who would touch it. It was just way too expensive, and risky from their standpoint. Oh, god, you put $100 a foot into something and then two years later it's shuttered. So as part of my McKinsey work I had consulted for Trammel Crow. And by 1980 Trammel Crow was one of the largest commercial real estate developers in America. So, I called Trammel at his headquarters in Dallas. And I said, in fact he had asked me at the end of our study to become his partner in New Jersey, in the real estate business. And, I told Trammel, I, "It's not my deal Trammel. I like science." Anyway, I called him up and I said, "Trammel, I need help." I said, "We've got this company. We've raised a pretty good chunk of money. We've got these high-tech products, and we need a plant, and it's going to be expensive, and I wonder if you'd do it?" So, he called his, his partner out here, Steve Williams, who was at that time very junior. Now, you know now we're all either gray haired or bald. And, Trammel said to Steve, "You know, Greene's a good guy. Let's do this." Right. So, they built this little tilt-up building, hardly as big as, you know, this clubhouse, in footprint, and helped us, you know, finance all the plumbing and everything else. Well, by the time Lilly bought us, Trammel Crow had over 250,000 square feet leased to Hybritech. Okay? Big deal. I mean, for all I know it made Trammel Crow, in San Diego, and when everybody else saw this going on all of a sudden when somebody would come to them with this biotech idea they were willing to do it. And, in fact, some people even started building sort of incubation centers, where they'd set up a lab in a modular way so that little companies could come and rent pieces of it. That was one story. Another story was, we needed a checking account. We had $300,000 and none of the banks wanted to touch us. This was before banks got into securitization of mortgages. And finally, either Brook or Tom called the local B of A branch that they were, you know, dealing with there in San Francisco and said, "Come on we got this little company and we want . . . " So, the

headquarters calls the La Jolla office and says, "Do it." The La Jolla office looks around and says, "All right, who is . . ." and Martha Dempski had just arrived from Chicago Business School, and they said, "Ah, Martha, we have a project for you." And I can just see the conventional bankers going, "Gees. I hope this doesn't turn into a turkey." Again, by the time Lilly bought Hybritech Martha had become the preeminent banker in Southern California for biotech. So, what was happening during these Hybritech years is people watched Hybritech explode. We had 800 employees when Lilly bought us. All of these various support groups prospered. We were working with Pillsbury, the law firm, and pretty soon our billings were right through the roof. We were doing IPOs, secondaries, corporate deals. I mean, the contract work and everything else. Ernst & Young was our auditor and pretty soon the audit fees were enormous. Okay? And so, all of these other support industries were watching this going on and they all began to decide they needed a Biotech Division. So, what that did was it made the environment here in San Diego very conducive to setting up shop. And you can add to that that we had literally recruited the best and the brightest out of not only the device industry but the therapeutics, drug industry. These people were all capable of doing their own thing

SHINDELL: And it seems like once they got, once they got here they didn't want to leave?

GREENE: Yeah. Well, sure. San Diego's not a bad place to live if you, if you weren't trying to buy a house in the last five years. But, I think the locals tend to overplay the relative desirability.

SHINDELL: That's just what keep hearing over and over again in the interviews is, "Once I got here I wasn't going to go back to St. Louis," or wherever it was they were coming from.

GREENE: Yeah. Well, certainly. First of all, of course, the weather is nice here, but ah, you know, weather, I don't think that's a big factor. What was a big factor is that there was so much enthusiasm and support for high tech ventures. If you lived in San Diego you'd go to a cocktail party: if you weren't involved with some sort of a neat high-tech startup you were just kind of an average Joe. Back in Chicago, if you weren't working for Sears Roebuck, United Airlines, whatever, you really must not have what it takes. Okay? Very, very different cultural philosophies. And, I've always thought

that one of the key sort of sociological factors for the success of biotech here in San Diego was that sort of attitude about entrepreneurialism.

SHINDELL: Are there any individuals that you would say were like key individuals who contributed to that local attitude or atmosphere? A lot of people mention Bill Otterson, for example, as being sort of key to fostering that.

GREENE: He was the, he was sort of the master of ceremonies. In other words, it was kind of like a, variety show where you had a whole bunch of stars coming in and doing great things. And Ed Sullivan would say, "Now, we're welcoming the Beatles." And, that's what Bill did and he did a great job. I mean, he got us together. He really started to form a voice for the industry. One of the things he did is open up UCSD. The UC system is a public employee system, very bureaucratic, very risk-averse. Most of the people who work there are socialists, I think. [Laugh] So, they were very standoffish and leery of these entrepreneurs who, from their standpoint, were out to make money. And, one of the things Bill did was to sort of provide a way to communicate. He asked me to give a speech to the faculty to talk about what we little companies do. And so, I put together some slides and one of the things I did is I put up a picture of a prospectus, our most recent public offering. And, I said to the group of professors. I said, "Now, this is how we do it. Okay?"

I said, "This is our grant proposal. That's exactly what it is," and you could see light bulbs. And, Bill said, "Boy, that was great." He said, "You would be surprised at how all of a sudden they began to understand that you were basically doing the same thing they were. It was just, institutionally somewhat different, but basically you're out raising money to pursue science. And, in your case if it's successful you end up with a product or a patent. In their case, if it's successful they end up with a, you know, a publication, and maybe a Nobel Prize." So, you know, and that's what Bill did real well. He was great at that.

SHINDELL: These days, I think, the people in the life sciences at UCSD are far more accepting of biotech and even eager to participate?

GREENE: Well, they've seen a lot of their colleagues move to the highest point in Del Mar and a big house.

SHINDELL: And it seems like the skepticism surrounding it has sort of faded away?

GREENE: It has. Well, there are still hardcore academics, as I say. The more leftist leaning who just fundamentally don't trust private industry, that's all. It's a physiological thing I guess. But, yeah, I would say, and in fact I saw this going on at Oxford when we were starting Amylin. And, the UC system had actually become especially since Boyer and Cohen's patent was rolling the cash in. That's the gene-splicing patent. And, the trustees and everybody else figured out, "Hey, this is a good idea, if our folks invent something really useful and we put it into a reasonable licensing agreement, those very, very few that actually succeed can generate huge returns for the university." Meanwhile Oxford ran about ten years behind on that, and when we got to Oxford and started looking for a place to build a lab and to get help from the faculty, I mean, it, they were really hostile. Whew. There was one, one, one academic – actually, there were a couple of academics who were very helpful to us at the senior level, Ed Southern, who ran the biochemistry labs. The other one that was, Jack Baldwin, who was the head of chemistry. And, in fact, he had done a lot of consulting for the pharmaceutical industry and he had a very good fundamental understanding of what the role of industry was. We started our first operation there in Oxford, in the labs, and when it came time to really set up our own facilities we couldn't. So, we moved over to San Diego, and I remember Jack Baldwin got up and, and made quite a noise in Oxford about how stupid they were to, to be driving these little ventures out. Today, they have a science park and that attitude has changed completely. The other thing that's happened is when Kohler and Milstein discovered the hybridoma process to make monoclonal antibodies, my understanding is they sent a, a disclosure to the Patent Office of the Medical Research Council, the MRC, and the lawyers there looked at it and said, "Hey, that's not patentable." Bad decision, because if they had patented it they would have had the same kind of a revenue stream that UC and Stanford got from the gene-splicing patent. One interesting anecdote on that is that the Amylin discovery was made at Oxford, and so the MRC was involved. One of my early things was to go to the MRC office in London where I met the head of Licensing. And, it was a very interesting meeting because Hybritech had basically taken the Kohler-Milstein technology and run like mad with it. The MRC was getting nothing from it. And so, when the licensing lady walked into the room she looked at me and she said, "I know who you are." Anyway, at least I had credibility. You know, those were the early days before the academics really figured it out.

SHINDELL: Well, it seems like even in the U.S., patents, the sort of ways that the patent system worked weren't exactly, it wasn't obvious how biotech patents would work at first?

GREENE: Yeah. It was real easy at first. I mean, where it became all garbaged up was when they got under this Genome Project and they started sort of patenting genetic sequences when there was very little evidence as to why they were useful. That's when it became controversial. In the early days, you know, either process patents or patents of molecules and so on were perfectly reasonable because, you know you had an idea of, of how to make a product out of it and you put that into your patent. Then you just argued with the Patent Office on what kind of breadth you should get for that patent. But until the '90s there was no confusion. What happened in the '90s is these guys are, you know, sequencing, sequencing, and they're generating thousands of these sequences, hundreds of thousands, and then they're, they've got sort of a template set up and they're dropping the sequences in and they're just shoveling applications into the Patent Office. And, that's when it hit the fan because it overloaded the system. Secondly, it really wasn't fair. So, that's when they began rethinking what is patentable.

SHINDELL: I wonder if you could talk a little bit more about the way that things have changed as this cluster has developed? Like, how has the biotech industry changed, or how has the situation for small startup companies changed?

GREENE: Well, I'll tell you one thing that's changed dramatically, and that is investors are no longer naïve about how magical biotech is going to be in generating spectacular drugs. You know, back when we started Amylin, there was this view that the whole notion of biotechnology, in other words using natural molecules and natural, harnessing natural biological processes was, was a tremendous breakthrough in the field of medicine and whereas all of the years of searching for small molecules and having to produce 100,000 of them to have even one that might work and not be toxic, that all of a sudden biotechnology was going to speed everything up, and reduce the risk. And so, you know, this naiveté allowed, like we went public basically just at the start of Phase I clinical trials with a $400-$500 million market cap. No more. There's now plenty of experience with how difficult these biotech projects are, and the one thing that has changed dramatically is that you can no longer start a company, at least with professional funding from VCs or whatever, unless you have very convincing proof of principle.

SHINDELL: It seems like you almost have to be ready to go to clinical trials?

GREENE: I'd say even more than that. You'd better have some, you know, human data. There are still a few VCs around that'll throw a couple hundred thousand at something. I'm working with a dear friend from Amylin on exactly that kind of a project, where he's got a hypothesis for treating diabetes and obesity, which has probably got a one in ten shot of really working, but it's sufficiently intriguing and from our standpoint fits right. You know, it's, regardless of what happens it's going to be useful scientific information, okay? And so, we've decided to just fund it ourselves. And, along with help from a local VC who's willing to, you know, to just roll the dice like this for small amounts of money. And what we've managed to do is, to keep it a virtual company, we are now starting clinical trials in Dubai. And, they're going to be a tenth of the cost of clinical trials, you know, in the more formal way they're done here. We will get some human data. It'll be valid, controlled data. It'll be early data. But, the main thing it'll be is if we see evidence of a relevant therapeutic effect it'll put us in a position to raise money. If we don't, hey, it was worth trying. I see this more and more, people are starting to look outside the U.S. for lower-cost ways of generating data, because the data is critical. Without human data you're not worth much, because the investors have now learned, after twenty years of shoveling money into biotech holes that human data makes all the difference.

SHINDELL: It seems like people are also going out, out of the country for producing products, as well.

GREENE: Yeah, well, not so much. Amylin is just completing a $550 million plant just north of Cincinnati. And, I'll tell you what, we would not have invested $550 million in a plant in Mexico, or India, or something like that. That being said, there are some extremely effective companies in this field, particularly in India, and everybody I know is, is starting to collaborate with them, because they do great science at a fraction of the cost. That swept through the computer business a decade ago and it's just now that the biology business has started to go the same way.

SHINDELL: Yeah. No, I think it was Jay Short who I was interviewing who said that he's setting up operations in China in a couple of different locations?

GREENE: Jay's a very smart guy. See, now there's a leader, he's a scientist. In fact, I remember when he and I first met each other it was a lunch. I think the lunch went on for two and a half hours. They were actually putting away the tables in the

restaurant and they shooed us out. And, he's the only guy I've ever known who pulled out his wallet and pulled out a picture of a molecule and said, "Look at this." He may have also had his kids in his wallet, but he had this molecule in his wallet. And that's, and I knew right then, "Ooh, he's my kind of guy." Okay? That's what it takes. The problem was, in a sense, that they were too successful too fast.

SHINDELL: How so?

GREENE: Well, Jay's timing was, couldn't have been better. He did his IPO right at the peak of the huge 2000 bubble, when the computer, the Internet stuff had gone through the roof. I think investors were starting to get worried about those valuations and they were looking for the next hot item, and they suddenly decided, "It's biotech." And, I'll tell you, man, just wham, up it went. And, so Jay's company went public at a multi-billion-dollar valuation. I think they raised like $800 million. I don't recall. All I know is that the numbers were just staggering. And, the problem with that was that the expectations are staggering. And, the realities of, of the world are that only rarely are you onto a technology where there aren't going to be delays, and problems, and stuff like that, and if investors have invested in you at a very high value and then your value falls – which they all did. I mean, they all collapsed after that – suddenly you're selling for a tenth or a fifth of what the investors came in at and you're tarnished goods. I mean it, that's bad for a company. But, Jay's a really good guy.

SHINDELL: Yeah. He was a very, very nice guy to interview I think. So, we're probably about out of time?

GREENE: Yeah. I think. I'm, I apologize but I've, I'm, as I say, on a scramble to get out of town.

SHINDELL: Okay. Well, I'd love to do a follow-up,

GREENE: Okay.

SHINDELL: ...if you're coming back this month?

GREENE: Well, let's, we can – I'll be back next week and then here for a couple of weeks.

SHINDELL: Oh, okay.

GREENE: I've got weddings. Then I'm gone. We live in Michigan now, and, we've got to get home.

SHINDELL: All right. Well, if you want to send me an email with your available dates, then, then-

GREENE: Okay.

SHINDELL: I'm sure we can set something up. All right. Great.

GREENE: Terrific.

SHINDELL: Well, thank you very much.

GREENE: Here's your – this thing. [Referring to microphone]

END INTERVIEW

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The San Diego Technology Archive (SDTA), an initiative of the UC San Diego Library**,** documents the history, formation, and evolution of the companies that formed the San Diego region's high-tech cluster, beginning in 1965. The SDTA captures the vision, strategic thinking, and recollections of key technology and business founders, entrepreneurs, academics, venture capitalists, early employees, and service providers, many of whom figured prominently in the development of San Diego's dynamic technology cluster. As these individuals articulate and comment on their contributions, innovations, and entrepreneurial trajectories, a rich living history emerges about the extraordinarily synergistic academic and commercial collaborations that distinguish the San Diego technology community.