Howard Greene

Interview conducted by

Matthew Shindell, Historian, UCSD

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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

INTERVIEWEE: Howard (Ted) Greene

INTERVIEWER: Matthew Shindell, Historian, UCSD

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

26 sometime earlier where they were presented. At the same time that I was being let go the
27 decision was made to move the division back to Chicago. And so, a group of other employees,
28 scientists, marketing people, and whatnot, in addition to myself, had decided we didn't want
29 to go back there so we set about starting a company to produce monoclonal antibodies. We
30 hooked up with a professor at UC Irvine, whose name happens to be Jim Watson. It's not of
31 Watson and Crick. And anyway, we rented a lab space next to where the division of Baxter
32 was located, started buying equipment from Baxter, because they were closing down their
33 labs, and I set out looking for money. I made presentations to several companies, Beckman in
34 the local area. Centex in the Bay Area. And I was, just to hedge my bet, kind of paying
35 attention to potential jobs, because, , startups are iffy things. Anyway, our startup company
36 was called Cytex and our first goal was to raise some money so that we could actually
37 function. Meanwhile, I got a call from a headhunter who was looking for a marketing position
38 for a new startup company called Genentech. And, when he described what they were trying
39 to do in the gene splicing area my reaction was, "Aha! They're into so-called genetic
40 engineering," (I don't think the term had even been invented yet) "and maybe I can learn
41 something from them, or maybe I want the job." So, I went up to San Francisco and spent a
42 day with Bob Swanson, who was the founder and CEO. With his gang I got along great, and I
43 told Bob I really wanted to start my own company. It wasn't competitive. He called me that
44 night and said, "You know, you'd be great for my marketing job, but even better for something
45 my partner Brook Byers is working on. He wants to start a company to make monoclonal
46 antibodies." Uh oh. I didn't let on that that's what I wanted to do, but you know, because my
47 partners and I had agreed we ought to keep it confidential. The next day Brook called. He was
48 the junior partner at Kleiner Perkins, and informed me that he was starting a company in San
49 Diego, called Hybritech. In fact, I think they had just, the week that we got together was the
50 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

76 represented a strong academic base and at that point that was really all we could draw from.
77 We were hiringjunior scientists right out of academia. Anyway, I think if you put timelines on
78 it, my pink slip arrived in early July of 78, I met Brook in probably October of '78, which is, I
79 think that's the official founding of Hybritech. In fact, we just had our, our thirtieth
80 anniversary.

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

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

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

86 **GREENE:** I'd gone to a conference. Again, I was operating in the diagnostic business and
87 antibodies were an important reagent that was used in a variety of tests, pregnancy tests,
88 serology tests, things like that. And, one of the speakers was Bill Dryer, who at the time was
89 at Caltech and may still be. And, he got up in front of this conference. It would have been,
90 about '76 or '77 is when I went to this conference and Bill Dryer got up in front of us all and he
91 says, "Look, I have a speech that was prepared to talk about fluorescent tagging of antibodies,"
92 meaning antiserum, "but," he says, "I'm going to drop that subject because," he said, "the
93 greatest breakthrough in the history of, of, you know, antibody technology has just been made
94 in England. It's called 'monoclonal antibodies.'" And, he proceeded to make his own
95 predictions about how this was going to absolutely revolutionize the use of antibodies in all
96 sorts of medical products. And, at the time I was pretty darn impressed. In fact for years after
97 at Hybritech we used to invite Bill to stop by on his way to his Mexican cottage. And, we
98 referred to him as Buck Rogers because Bill's mind was always five years ahead. He foresaw
99 genetic engineering of monoclonals at least five years before the firstsuccessful attempts were

100 made. And, so that planted it firmly in my mind. When notice came from Baxter that I was a
101 short-timerin conversations with one of our scientists, it turned out he was interested in
102 monoclonals also and knew Jim Watson at UCI. We went to Watson's lab, and he showed us
103 how he did it, which wasnot very complicated. In other words, it didn't requirespaced age,
104 sophisticated laboratory, just a protein chemistry or a cell biology lab. So, by the time he was
105 through demonstrating it I figured, "Hey, we can do that," so, we went down to the UCI
106 cafeteria or whatever it is and ordered a pitcher of beer, and by the second or third pitcher of
107 beer we had all decided, "Let's start a company." So, you know, that's basically how it came
108 about.

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

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

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

117 **GREENE:** Most of the knowledge was in academia. Okay? I mean it was, it was a hot, hot
118 thing in academia. Ivor got into it because his field is cancer, particularly blood cancers. And
119 he, along with a number of other people realized that one of the things you could do by
120 cloning antibodies this way was to raise antibodies to antigens which are proteins on the
121 surface of cells that would be impossible to do by trying to isolate these proteins and inject
122 them into animals to stimulate an immune response. Instead, what you did is you just
123 immunized a mouse with the whole protein gemish 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 withventure 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

148 airport where basically Tom and Brook had come down here to go through the lab with Ivor
149 and o Tom said, "Look, here's what we'll do. We'll give you $300,000 for sixty percent of the
150 company. You take the $300,000 and if by the time you've mostly run out of it there's
151 something here, we'll go from there. If not? Well, no hard feelings. But, it looks like an
152 interestingproject for us." Which, I think is reflective of the way venture capital used to be
153 done. There was nomassive business plan.) It was just sort of, "Well, let's seed this thing
154 with a little bit of money, see if these guys can actually start to put something together that
155 will, looks like it's leading somewhere. And if they do we'll go raise real money. And, if they
156 don't, eh, $300,000." After all those guys probably spent more than that on their annual rent
157 since they were in downtown San Francisco. So, by the time I came aboard they were about
158 the two hundred, of the $300,000 left. I was paying myself $40,000, which was a big cut in pay
159 from Baxter. So there wenta good chunk of it. So, I updated my original business plan. My
160 business plan was very different than Ivor's, and I think this is what intrigued Tom. I was
161 promoting the notion that these antibodies would make it feasible to produce much more
162 useful products. In other words, products that could not be made with conventional
163 antiserum that now could be made with, with these monoclonals. Better diagnostics,
164 therapeutics, and basically my business plan was to put together proprietary products and
165 charge a premium for them. And, I think that intrigued Perkins and Byers. At Stanford, we'd
166 go through this two-part case and Ivor would come up for the first day to give all the
167 background (and I'll let him, corroborate my memory), and then I'd come up the next day and
168 at that point it was a sort of a big investment decision, all of the $ 1,600,000 million was what
169 we raised. Back then that was, enormous! And, the students would go through the whole
170 thing. But for me the, the real lesson from it was that my business plan focused on, on
171 inventing novel new products and charging a premium for them which was more attractive in
172 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 – becausethey'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 i 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 wasMonte 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 isthe top five percent or something, so I got lots of job offers. In factI think I made trips to twenty-one

193 different companies. Just dumb. I didn't know what the heck I wanted to do. And, I got an
194 offer from McKinsey and Company, which struck me as a pretty, pretty classy outfit, and they
195 would put me in the Chicago office so I could send the family to Michigan for summers. And, I
196 decided that was a way to take a job without making an decisions about what I wanted to do.
197 So, I was with McKinsey for seven years. In fact, I basically was a pioneer at McKinsey in using
198 computer modeling for, business plans and that kind of thing. And, I was using GE
199 Timesharing at the time, because there was no, you know, PC, or anything like that. Anyway,
200 one of my clients was Baxter. At the time Baxter's CEO was a man named Bill Graham, who to
201 this day I think is the most accomplished, tremendous CEO I've ever known or worked with.
202 And, he had a very interesting philosophy in management and that was he simply hired the
203 best and the brightest and the most ambitious people that he could hire and thencreated
204 something for them to do. He didn't have a sort of a list of job openings. And, in fact, a
205 professor at Harvard, Monica Higgins, has written a wonderful analysis of the Baxter
206 management style. It's called *Career Imprints*. She basically was trying to answer the
207 question of why Baxter alumni were so overrepresented among the biotech CEOs. She has
208 data showing that when you compare Baxter, based on its size, to Merck, and Abbott, and
209 some of the others, J&J, that Baxter was the prime source of biotech CEOs. I think for me the
210 combination of McKinsey and Baxter was great. McKinsey was an extremely analytically-
211 oriented environment where I ended up doing a lot of strategic planning, very analytical
212 planning. I was trained thoroughly in communications skills, because in the consulting
213 business, you know, maybe half the job is to figure out what the client should do, but the other
214 half of the job is to convince them to do it. And so, they have to this day a tremendous editing
215 capability and all, there is just no better training in how to communicate than McKenzie, or
216 BCG or whatever. This served me extremely well when it came time to go out and start
217 pitching Hybritech's business plan, going to Wall Street and so on. I was ready. The other

218 thing, of course, was Baxter's management style, namely this philosophy of bringing really,
219 really bright people in and pushing responsibility onto them way sooner than their age and
220 career experience would, would suggest. And the good ones rose to the occasion. Higgins'
221 book is full of anecdotes. It focuses on Gabe Schmergel, who was made the general manager of
222 Germany, I think, at the age of 29 or something like that. But, that was Bill's philosophy. And,
223 I carried that philosophy to Hybritech. We just had this reunion and, and you know,
224 everybody's talking about, a lot of the people there said, you know, "Never again have they
225 ever worked for a company that was as much fun as Hybritech." And, I really think it was that
226 management philosophy of, you know, hire the best and the brightest and give them
227 responsibility that was what made us so successful.

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

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

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

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

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

264 **SHINDELL:** Would the sort of corollary to that be that a conservative startup company just
265 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 havean 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 companymanagement 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 thatwhen 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 nothingat the time, that specialized in that sort of thing. And, at one point they were printing business cards, he said, and they had tocome 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

313 starting a venture capital firm in San Francisco. So, he called Tom up and said, "Look, next
314 time you're in New York stop by and let's get acquainted." So, Tom did. And, after I suppose
315 they had lunch together or something like that, Benno said, he said to Tom, "Look, I'm working
316 out here on the East Coast. You're working on the West Coast. How about when I get
317 something interesting here I'll give you a call to see if you want to participate and visa versa?"
318 So, time goes by and Benno's on a business trip to Japan and Tom calls J.H. Whitney to speak
319 to Benno. He gets shunted to a junior, partner, explains that he has this deal, a company called
320 Tandem Computers, (which turned out to be one of the all-time big hits of the late '70s), and
321 he thought maybe Benno would like to participate. And, so the junior associate said, "Fine.
322 Send us a business plan and we'll be back to you in thirty days." I've heard this story from
323 Benno probably three timesand at that point every single time Benno got tears in his eyes,
324 because he says, "You know, I never got a call back from Tom Perkins ever again." And,
325 basically what that reflected was the way business was done between Perkins and Art Rock
326 andPitch Johnson, and so on. They would eachstart to sponsor their own little startup.
327 Another anecdote. This case study that Pitch taught at Stanford. One time I was there and he
328 was going through discounted cash flows. He had my financial projections and he wastrying
329 to show the class how you do an internal rate of returnand figure out whether it looks like a
330 good investment at whatever value. And, when he got done with it I said, "Pitch, can I ask a
331 question?" He said, "Sure." This is in front of the class. And I said, "You were a real early
332 investor in Hybritech, weren't you?" And he says, "Yup." And I said, "Well, why did you
333 invest?" And he said, "Well, Brook called me up and said it was a good idea." And he suddenly
334 realized what he'd just said and he went, "Ha!" Because he'd just completely undone all of his
335 rigmarole about, you know, return on investment. And, I think what's, what's happened and
336 one of the sad things about venture capital now is that it is so institutionalized that that's what
337 they do: they work their spreadsheets and they work out their IRRs and all this kind of stuff,

338 and their deal structures have become so complicated that even they don't really understand
339 them, and it's just a very different thing.

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

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

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

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

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

355 **GREENE:** Certainly relative. The thing that I would love to see is some sort of a measure of
356 biotech's importance relative to the other high-tech industries here in San Diego. In the Bay
357 Area there are, there's probably more employees, engaged in biotechnology but relatively
358 speaking it's less important. because, they have the whole Silicon Valley, you know, whether
359 it's the hardware or software, or whatever. But here in San Diego, biotech's a big deal.

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

362 **GREENE:** Well, there are a number of ways. First of all, Hybritech was a great role model.
363 And, I remember when we first started we tried to rent everything because we didn't want to
364 buy anything. And, real estate was something we needed. We needed wet labs, which at the
365 time cost over $100 a square foot, when most of the developers were looking at maybe $15 a
366 square foot. So, when we got ready to build our first plant to make product we couldn't find
367 any local developers who would touch it. It was just way too expensive, and risky from their
368 standpoint. Oh, god, you put $100 a foot into something and then two years later it's
369 shuttered. Soas part of my McKinsey work I had consulted for Trammel Crow. And by 1980
370 Trammel Crow was one of the largest commercial real estate developers in America. So, I
371 called Trammelat his headquarters in Dallas. And I said, in fact he had asked me at the end of
372 our study to become his partner in New Jersey, in the real estate business. And, I told
373 Trammel, I, "It's not my deal Trammel. I like science." Anyway, I called him up and I said,
374 "Trammel, I need help." I said, "We've got this company. We've raised a pretty good chunk of
375 money. We've got these high-tech products, and we need a plant, and it's going to be
376 expensive, and I wonder if you'd do it?" So, he called his, his partner out here, Steve Williams,
377 who was at that time very junior. Now, you know now we're all either gray haired or bald.
378 And, Trammel said to Steve, "You know, Greene's a good guy. Let's do this." Right. So, they
379 built this little tilt-up building, hardly as big as, you know, this clubhouse, in footprint, and
380 helped us, you know, finance all the plumbing and everything else. Well, by the time Lilly
381 bought us Trammel Crow had over 250,000 square feet leased to Hybritech. Okay? Big deal. I
382 mean, for all I know it made Trammel Crow, in San Diego, and when everybody else saw this
383 going on all of a sudden when somebody would come to them with this biotech idea they were
384 willing to do it. And, in fact, some people even started buildingsort of incubation centers,

385 where they'd set up a lab in a modular way so that little companies could come and rent
386 pieces of it. That was one story. Another story was, we needed a checking account. We had
387 $300,000 and none of the banks wanted to touch us. This was before banks got
388 intosecuritization of mortgages. And finally, either Brook or Tom called the local B of A
389 branch that they were, you know, dealing with there in San Francisco and said, "Come onwe
390 got this little company and we want . . . " So, the headquarters calls the La Jolla office and says,
391 "Do it." The La Jolla office looks around and says, "All right, who is . . ." and Martha Dempski
392 had just arrived from Chicago Business School, and they said, "Ah, Martha, we have a project
393 for you." And I can just see the conventional bankers going, "Gees. I hope this doesn't turn
394 into a turkey." Again, by the time Lilly bought Hybritech Martha had become the preeminent
395 banker in Southern California for biotech. So, what was happening during these Hybritech
396 years is people watched Hybritech explode. We had 800 employees when Lilly bought us. All
397 of these various support groups prospered. We were working with Pillsbury, the law firm, and
398 pretty soon our billings were right through the roof. We were doing IPOs, secondaries,
399 corporate deals. I mean, the contract work and everything else. Ernst & Young was our
400 auditor and pretty soon the audit fees were enormous. Okay? And so, all of these other
401 support industries were watching this going on and they all began to decide they needed a
402 Biotech Division. So, what that did was it made the environment here in San Diego very
403 conducive to setting up shop. And you can add to that that we had literally recruited thethe
404 best and the brightest out of not only the device industry but the therapeutics, drug industry.
405 These people were all capable of doing their own thing SHINDELL: And it seems like once
406 they got, once they got here they didn't want to leave?

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

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

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

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

423 **GREENE:** He was the, he was sort of the master of ceremonies. In other words, it was kind of
424 like a, variety show where you had a whole bunch of stars coming in anddoing great things.
425 And Ed Sullivanwould say, "Now, we're welcoming the Beatles." And, that's what Bill did and
426 he did a great job. I mean, he got us together. He really started toform a voice for the
427 industry. One of the things he did is, , open up UCSD. The UC system is a public employee
428 system, very bureaucratic, very risk-averse. Most of the people who work there are socialists,
429 I think. [Laugh] So, they were very standoffish and leery of these entrepreneurs who, from
430 their standpoint, were out to make money. And, one of the things Bill did was to sort of
431 provide a way to communicate. He asked me to give a speech to the faculty to talk about what
432 we little companies do. And so, I put together some slides and one of the things I did is I put

433 up a picture of a prospectus, our most recent public offering. And, I said to the group of
434 professors. I said, "Now, this is how we do it. Okay?" .

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

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

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

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

447 **GREENE:** It has. Well, there are still hardcore academics, as I say. The more leftist leaning
448 who just fundamentally don't trust private industrythat's all. It's a physiological thing I guess.
449 But, yeah, I would say, and in fact I saw this going on at Oxford when we were starting Amylin.
450 And, the UC system had actually becomeespecially sinceBoyer and Cohen's patent was rolling
451 the cash in. That's the gene-splicing patent. And, the trustees and everybody else figured out,
452 "Hey, this is a good idea, if our folks invent something really useful and we put it into a
453 reasonable licensing agreement, those very, very few that actually succeed can generate huge
454 returns for the university." Meanwhile Oxford ran about ten years behind on that, and when
455 we got to Oxford and started looking for a place to build a lab and to get help from the faculty,

456 I mean, it, they were really hostile. Whew. There was one, one, one academic – actually, there
457 were a couple of academics who were very helpful to us at the senior level, Ed Southern, who
458 ran the biochemistry labs. The other one that was, Jack Baldwin, who was the head of
459 chemistry. And, in fact, he had done a lot of consulting for the pharmaceutical industry and he
460 had a very good fundamental understanding of what the role of industry was.We started our
461 first operation there in Oxford, in the labs, and when it came time to really set up our own
462 facilities we couldn't. So, we moved over to San Diego, and I remember Jack Baldwin got up
463 and, and made quite a noise in Oxford about how stupid they were to, to be driving these little
464 ventures out. Today, they have a science park and that attitude has changed completely. The
465 other thing that's happened is when Kohler and Milstein discovered the hybridoma process to
466 make monoclonal antibodies, my understanding is they sent a, a disclosure to the Patent
467 Office of the Medical Research Council, the MRC, and the lawyers there looked at it and said,
468 "Hey, that's not patentable." Bad decision, because if they had patented it they would have
469 had the same kind of a revenue stream that UC and Stanford got from the gene-splicing patent.
470 One interesting anecdote on that is that the Amylin discovery was made at Oxford, and so the
471 MRC was involved. One of my early things was to go to the MRC office in London where I met
472 the head of Licensing. And, it was a very interesting meeting becauseHybritech had basically
473 taken the Kohler-Milstein technology and run like mad with it. The MRC was getting nothing
474 from it. And so, when the licensing lady walked into the room she looked at me and she said,
475 "I know who you are." Anyway, at least I had credibility. You know, those were the early days
476 before the academics really figured it out.

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

479 **GREENE:** Yeah. It was real easy at first. I mean, where it became all garbaged up was when
480 they got under this Genome Project and they started sort of patenting genetic sequences

481 whenthere was very little evidence as to why they were useful. That's when it became
482 controversial. In the early days, you know, either process patents or patents of molecules and
483 so on were perfectly reasonable because, you know you had an idea of, of how to make a
484 product out of it and you put that into your patent. Then you just argued with the Patent Office
485 on what kind of breadth you should get for that patent. Butuntil the '90s there was no
486 confusion. What happened in the '90s is these guys are, you know, sequencing, sequencing,
487 and they're generatingthousands of these sequences, hundreds of thousands, and then they're,
488 they've got sort of a template set up and they're dropping the sequences in and they're just
489 shoveling applications into the Patent Office. And, that's when it hit the fan because it
490 overloaded the system. Secondly, it really wasn't fair. So, that's when they began rethinking
491 what is patentable.

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

495 **GREENE:** Well, I'll tell you one thing that's changed dramatically, and that is investors are no
496 longer naïve about how magical biotech is going to be in generating spectacular drugs. You
497 know, back when we started Amylin, there was this view that the whole notion of
498 biotechnology, in other words using natural molecules and natural, harnessing natural
499 biological processes was, was a tremendous breakthrough in the field of medicine and
500 whereas all of the years ofsearching for small molecules and having to produce 100,000 of
501 them to have even one that might work and not be toxic, that all of a sudden biotechnology
502 was going to speed everything up, and reduce the risk. And so, you know, this naiveté
503 allowed, like we went public basically just at the start of Phase I clinical trials with a $400-
504 $500 million market cap. No more. There's now plenty of experience with how difficult these
505 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 informationokay? And so, we've decided tojust fund it ourselves. And, along with help from a local VC who'swilling 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. (Shindell: Uhm-hmm.) 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 ofshoveling money into biotech holes thathuman data makes all the difference.

SHINDELL: It seems like people are also going out, out of the country forproducing 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 agoand it's just now that thethe 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 actuallyputting 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 thatonly 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.) 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.) 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), UC San Diego Library, La Jolla, CA.

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.