Ivor Royston

Interview conducted by

Matthew Shindell, Historian

October 14, 2008

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Ivor Royston

Dr. Ivor Royston, M.D. is a Managing Member at Forward Ventures II, IV and V L.P. Dr. Royston has been involved in the biotechnology industry from its inception in 1978 with the founding of Hybritech, Inc. and of Idec Pharmaceuticals in 1986. He has been instrumental in the formation, financing, and development of numerous biotechnology companies, including Corixa and, Genstar Therapeutics. Dr. Royston Co-founded Beckman Coulter, Inc., Biogen Idec Inc., and GeneSys Therapeutic Corp. He is the Founding Chairman of Quantum. He served as the Chairman of Corautus Genetics Inc. from April 1997 to August 1998. Dr. Royston served as Chairman of Deltagen Research Laboratories, L.L.C., Imagine Pharmaceuticals, Inc., Morphotek, Inc., Sagres Discovery, Inc. and TargeGen, Inc. Dr. Royston served as Chairman of CancerVax Corp. since December 2000. He is a founding Director of Genesys Therapeutics, GenQuest, CombiChem, Sequana Therapeutics, Triangle Pharmaceuticals, Applied Molecular Evolution, and Variagenics. He serves as Director of HemaQuest Pharmaceuticals, Inc. and Syndax Pharmaceuticals, Inc. Dr. Royston has been Member of the Board of Advisors at MMRGlobal, Inc. since May 2010 and has been its Director since May 27, 2013. He serves as Member of the Board of Advisors of MyMedicalRecords, Inc. Dr. Royston serves as a Director of Arizeke. He has been Director of Biocept, Inc since April 11, 2011 and Avalon Pharmaceuticals, Inc. since August 2000. Dr. Royston served as Director of Conforma Therapeutics Corporation, LigoCyte Pharmaceuticals, Inc. and Altair Therapeutics, Inc. He served as its Director at MMRGlobal, Inc. from January 2000 to January 2009. He served as Director of VIA Pharmaceuticals, Inc. until June 05, 2007, Micromet, Inc. until May 05, 2006, Corautus Genetics Inc. since February 5, 2003 and Favrille Inc. since January 2000. Dr. Royston also served as a Director of Clinical Immunology Program at the UCSD Cancer Center and Chief of Oncology at the San Diego VA Medical Center. From 1990 until 2000, Dr. Royston was the President and Chief Executive

Officer of Sidney Kimmel Cancer Center (formerly the San Diego Regional Cancer Center). From 1977 to 1990, he held various positions in academic medicine and cancer center at the University of California, San Diego (UCSD) School of Medicine. Dr. Royston was on the faculty of the medical school and cancer center at the University of California, San Diego from 1978 to 1990. In 1997, President Clinton appointed him to a six-year term on the National Cancer Advisory Board. Dr. Royston is trained in internal medicine and oncology at Stanford University and is board certified in both Internal Medicine and Medical Oncology. He is a nationally recognized physician-scientist in the area of cancer immunology. Dr. Royston received an M.D. in 1970 from The Johns Hopkins University, a B.A. in Human Biology in 1967, and completed post-doctoral training in Internal Medicine and Medical Oncology at Stanford University.

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THE SAN DIEGO TECHNOLOGY ARCHIVE

INTERVIEWEE: **Ivor Royston**

INTERVIEWER: **Matthew Shindell**

DATE: **October 14, 2008**

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ROYSTON: Okay. Well, thank you Matt. My name's Ivor Royston. Does that sound, is the level good? Or . . .

SHINDELL: The level looks great. So, this is an interview with Ivor Royston. It's October 14, 2008. The interviewer is Matthew Shindell.

ROYSTON: Okay.

SHINDELL: Dr. Royston, if you could please tell us . . .

ROYSTON: How I got involved with . . .

SHINDELL: How did you get involved in San Diego biotech?

ROYSTON: Well, it goes back to when I came down to San Diego with Howard Birndorf, since you mentioned his name. So, let's go back to – I'm doing my – I mean, I don't know how far back you want me to go, but we'll, let's go back to the fact that in 1975-77 I was a postdoctoral fellow at Stanford Medical Center doing my oncology fellowship, which was required to ultimately become a board certified oncologist, which was my goal I had already completed internship and residency in internal medicine. I'd done research at the NIH, and there's some great stories there too, [Laugh] I have. And, and then, and then I finished up by doing my fellowship at Stanford. And, when I was at Stanford it was, and I had experience, as I mentioned, doing medical research, especially immunology and cell biology research at NIH in the years beforehand. An article appeared in *Nature* magazine which demonstrated the ability to make monoclonal antibodies. It was written by George Kohler, and Caesar Milstein, who ultimately, years later, won the Nobel Prize. And in that article,

they talked about how you could make antibodies in a cloned manner, a large number of highly-specific antibodies, which had never been done before. Because, in the old days if you wanted an antibody you would just bleed a goat or a sheep or, anyway, and so, you know, if you wanted an antibody to let's say to a virus you would inject the virus into an animal, the animal would make antibodies, and you bled the animal and you took out the serum and you would have antibodies. The only problem is, it was a mixture of all kinds of different antibodies, many, many hundreds of types of different antibodies and it would never be an unlimited amount of any given antibody. When Kohler-Milstein discovered that you could make unlimited amounts of a single antibody by using certain genetic engineering techniques that we call "cell fusion," it was analogous to the, the people who had cloned DNA and developed the recombinant DNA revolution, which is, as you know, the ability to make unlimited amounts of protein from a single DNA. This sparked the whole biotech revolution. So here, I saw the same potential and I realized, "Boy, if we can make unlimited amounts of a cloned antibody maybe we could develop antibodies as a new weapon for treating cancer. Remember I'm studying to be a cancer doctor and my goal was to be on the faculty of a major cancer center, and I realized at that point, while I was at Stanford that this was an area that I wanted to pursue. When I read the technology about how you did this, I said, "Well, I know how to do that. I can do this and do this. I've had that experience. And, I talked to Howard about it, who was working as a technician there and I started writing grants in anticipation of doing that, knowing that ultimately I'll be winding up at some place, some university. And so, where I ended up was getting an offer from UCSD to come and join the new cancer center that was being developed at UCSD in 1976 – by John Mendelsohn. This is the same John Mendelsohn that's now head of MD Anderson, who we just talked about. He was starting the Cancer Center at UCSD and was looking for several new faculty members to help him get started. And, I applied for that job and I was one of three that was chosen to head up the Center, and to be the head of clinical immunology. When John he interviewed me he said, "What do you want to work on?" I said, "Well, I want to make monoclonal antibodies to treat cancer." And, of course, nobody knew what monoclonal antibodies were. Dr. Mendelson went on to become the inventor of Erbitux, which is one of the major antibodies today that's used to treat cancer. So, I said to Howard, "Hey," you know, Howard I got to know him and we did some stuff together at Stanford. I said, "Why don't you come down with me to San Diego. I got the job. Why don't you come down to me, with me, and we'll work on this new technology for making monoclonal

antibodies?" So, first thing we did, we set up our lab and, in 1977 I took the job in July of 1977. It was many years ago now, right? That's what? We're already in '08 so that's thirty years ago we're talking about. It was back a long, time. So, we set up the lab. Howard was my chief technician. And, I said, "Okay, why don't we work on leukemia. Let's take some leukemia cells and show that we can make a monoclonal antibody that reacts with leukemia but does not react with normal white cells to show that we can get a highly specific antibody." And so, we're using the Kohler-Milstein technology. We went ahead and did this. Now, I have to, I'm going to diverge a little bit, more than I would normally for you because Clay (movie producer) is here. Because there are some real great vignettes and anecdotes that he'll be interested in them maybe more so than you. But, maybe I'm wrong. Maybe anybody would.

So, when you make these antibodies it's like making bread. You have to have yeast to make bread, right? To make these antibodies you need a cell line that you need to fuse with antibody-creating cells that you take out from the spleen of an animal, in this case mice, and you fuse them together and that, and you create what is called a hybridoma, a hybrid of both cells. So, the antibody cells from the spleen of the animal are programmed to make an antibody, but the cell line has the immortality factor n- it can grow forever. By fusing them together I created a cell line that could make a single antibody forever, that's the whole idea. So, the question people have often asked me when they talk about starting the industry down here is, "Well, where did the cell line come from, this specific cell line?" Well, it, this is a very interesting story, because in those days, in 1977, there was no such thing as an MTA, a Material Transfer Agreement. Today you can't send a biological cell line from one institution to another without signing an agreement that you won't commercialize it without the institution's approval. . So, here's what happened. When I got the idea at Stanford that I wanted to work on monoclonal antibodies for treating cancer, I knew that I needed the cell line, and the only cell line I knew was the one that was developed in, in England by Kohler and Milstein who later won the Nobel Prize. I found out that one of the professors at Stanford –

SHINDELL: Would you like me to pause it?

ROYSTON: No. That's all right. So, thirty years ago, this professor was at the laboratory at Kohler and Milstein on a sabbatical when the discovery was made, and while I was at Stanford. When he heard about this discovery he actually brought the

cell line back to Stanford. And,–then one of my colleagues in the oncology department at Stanford got a hold of the cell line and started to do some experiments, and then I also got a hold of the cell line from there. People were just – and, knowing that someday I was going to do this, and I had my own liquid nitrogen tank that I, even though I did not have a faculty position I had my own liquid nitrogen tank that I brought from NIH and parked in a professor's laboratory and made him a deal. I said, "Look, if you fill this up on a regular basis with liquid nitrogen to preserve it, I will let you share some of the cells that are in my liquid nitrogen tank." [Laugh] Because I, what I did was, when I was at NIH, before coming to Stanford, I had worked on a number of projects and I gathered a large number of what I, cell lines, which we kept in a frozen state in liquid nitrogen , and I felt that in my future career I might need those cells. So, what I did is I arranged to decommission the tank at the, at NIH. That's the words that they use in the government. To "decommission" means to get rid of it, and so I was free to take the tank with me. So, I took this liquid nitrogen tank in a truck and took it cross country from Bethesda, Maryland to Stanford, where I had my fellowship. So, I actually drove that tank [Laugh] full of liquid nitrogen and cells, personally, to Stanford as a young physician, knowing that I might need it someday. So, when I got to Stanford I had to have a place to put it. So, I went up to this doctor, I won't go into the names here, and said, somebody I got to know and befriended, and I said, "Look, I have hundreds of different cell lines here that you may want to use. I'll let you use them. Just do me a favor, keep this tank full with liquid nitrogen." He said, "Fine." So, when I found out that this Professor brought this cell line from – see, this is stuff that no one's ever documented before. When I found out that he had this cell line, that he had just visited Kohler and Milstein where this Nobel Prize winning discovery was made, that cell line was now at Stanford. So, I got a hold of it, because everybody, I mean in these labs there were people starting to work with it. I just took some, froze it down, put it in my cell tank, in my tank, that belonged to Ivor Royston. So, I now had the cell line in there. That's a long story, because when I moved to San Diego the tank followed me. [Laugh] So, when I moved I put the tank, the UCSD paid for the moving expenses, so I took my liquid nitrogen tank, put it on the moving truck, [Pages turning] and it moved it south from Stanford to San Diego. So, when I got to San Diego I just pulled out the cells, with Howard, and I'll bet you he didn't even tell you this story -- so, I pulled out the cells from the tank and we started saying, "Okay, we're going to start working on monoclonal antibodies." I had a grant from the NIH. We're going to start working on making monoclonal antibodies for leukemia. The

issue is you have to have those cells. So, okay. I wasn't the only one that had those cells. Those cells were actually distributed. I mean, if I had asked for them officially they probably would have sent it, okay? I mean, I'm just injecting a little humor about how I personally got the cells down. But, we get into a more serious issue about when I started the company Hybritech, how the cells got from UCSD to the company. That's a more serious issue, because there were no rules and regulations then. So at UCSD so we started out to make these antibodies to leukemia. Well, we were very successful. That's the nice thing about, about something that really works. We started doing the experiments and they started working just, you know, on schedule, and became very, you know, it worked really, really well. We took, we injected these leukemia cells into mice. We took the spleens out of the mice. We fused it with our cell line that I had just grown up from the liquid nitrogen tank that we know had worked, published in *Nature*, and we fused them and sure enough we had cells growing in culture that were making antibodies to leukemia cells. And then, the eureka moment was when we tested those antibodies we found out we could pick out antibody clones that reacted just with the leukemia cells and not with normal white blood cells. We were looking for that, what we call that tumor-specific antibody. And, I said "Howard, we've got it. This is fantastic. We can now go ahead and treat cancer, but how but how? How am I going to grow it up in large scale?" You know, you need to grow out from there. "How am I going to make gram quantities of the stuff and how am I going to purify it? How am I going to manufacture it? How am I going to do whatever?" I was stuck. But the idea was, "Yeah, but how do I get to the next step of implementation?" So, Howard would say to me, "Well let's, we'll license it to a company. Well, you know, let's go talk to a pharmaceutical company." So, I go talk to Eli Lilly, or, or Smith Kline, or whatever the companies were in those days, and, and they didn't know what I was talking about. And I said, "Well, I'm cloning these antibodies." Now, we're talking 1977, the end of '77. The invention was only made in '75 at, you know, people were not really I mean nobody, it was really still very early and people didn't , you know, couldn't relate to me. "What do you mean growing antibodies in a test tube?" You know, there was nobody that really understood what I was talking about. So, I said to Howard, "You know, when we were at Stanford, you know, when people had these great ideas they started companies, like Genentech, and my professor, John Daniels, started a company called Collagen. Maybe we just need to start our own company." And he said, "Okay. Let's do that." So, I said, "Well, you know, we're going to have to write a business plan or something," and so I went to the library and got a book

about how to write a business plan. But then, I had just gotten married and I married a woman that I had met at Stanford, who came down from Stanford and joined me. So, now I was married and she was a nurse at Stanford and we had had a relationship going on, and when I left to come to San Diego she still was at Stanford And I said, "Look, why don't you move down to San Diego so we can continue the relation[ship]. It's hard for me to get up there. I'm on the faculty at UCSD." And so she came down and we got married. Then one day I was talking to her about this whole thing, I said, "I think we ought to start a company because these pharma companies don't know what I'm talking about. We'll just start our own company, because we got to manufacture these antibodies, got to get them into patients if we want to cure cancer." I was only focused, at that time as a young investigator, you know, I was here, in San Diego to figure out a way to cure cancer. That's what my whole life was, from a, as an eight-year-old boy I was programmed to go into oncology, to go to medical school, to go into cure cancer.

SHINDELL: What drew you to oncology?

ROYSTON: The curiosity. The intellectual curiosity that no one knew anything about cancer. I had nobody who died of cancer in my immediate family. Later on my mother passed away from cancer when she was seventy-five, but when I grew up there were no cancer deaths in my family, except for a distant cousin, who had Hodgkin's Disease and died, but I didn't know him very well. But, it was more like when people talk about cancer, "Well, what is cancer?" You know, when they talk about it it's, "Well, cells are growing and killing." No one knew what – it was a black box and I was driven by the intellectual curiosity and felt that that's the next frontier in medicine – I knew I wanted to be in, go into medicine and that, that I had chose cancer. So, and it was only when this discovery was made that I chose to focus on, "Well, let's use this new technology for developing the magic bullets for treating cancer." So, I'm talking to my wife. My wife said, "Well, you know, I met this guy up in the Bay Area, you know. I dated him once and he called, he said he was, he called himself a 'venture capitalist.'" And, I had never heard the word "venture," I really didn't know what a venture capitalist was, which is the irony, right, then, because now [Laugh] we're venture capitalists. He knows that, because many, thirty years later I am a venture capitalist. [Laugh] And, but in those days I didn't know what a venture capitalist – I said, "Well, what do they do?" And she says, "Well, you know, they start companies, they invest in companies. That's how Genentech got started."

And so I said, "Well, maybe I should talk to one of these guys?" And, she says, "Well, okay, I know this guy Brook Byers." It's now Kleiner Perkins Caufield & Byers, which is the number one venture capital firm. I said, "Why not give him a call?" So, she calls him and she says, you know, "My husband's got this idea." And he said, "Well," just to be nice to her he says, you know, "He's going to be in San Francisco at a meeting can he stop by and talk to you or have lunch with you?" And, he wants to be, he's being nice to her because he had [Laugh] known her once before, or dated her once. He said, "Sure. Have your husband get in touch with me and stop by." So, I had this pivotal lunch in San Francisco and it would have been in the summer of '78. And, the reason I know that, because when, ultimately when he finally got involved it was October. Well, somewhere around, well maybe late spring, early summer of '78. But, we had made our, when we, when I moved to San Diego in July of '77 and set up my lab we had those results about, with the antibodies differentiating leukemia cells from normal white blood, so we had that like in about six months. It was really, we were very lucky, very fortunate. Things really worked out well, and Howard was my chief technician then. So, I met with Brook Byers, who was the junior partner, had just joined the firm a little bit earlier. He was trying to make a name for himself, and I obviously said all the right things at the lunch, because I said, "You know, Brook, nice to meet you and all that. You know, I have this idea," and I said, "you know, just like you can clone genes to make insulin," that's what they did at the time, "insulin and human growth hormone" – that's what Genentech had done in those days, – "you know, we can also clone antibodies now by using this new technology." So, that resonated with him, cloning genes and cloning antibodies. And I said, "Cloning antibodies will be just as big as cloning genes, because there are so many different things you could do with antibodies." So he got it, so when I made the analogy between what I was doing and the, and the success they had had with Genentech, because that was like a huge success at that time in 1978. It had already gone public, as I recall, in 1976. And, they had already been making insulin. He said, "Do me a favor. Write up this, what you just told me today. Write it up and send me a, a little outline or plan of what we just talked about here, and tell me how you think this would work, and what kind of a business you could make out of it, and let me think about it." So, I went home and talked to Howard and, actually that's when we got the business plan book from the library. I said, "We need write up this this 5 page document. That, that document still exists and the original is at the Chemical Heritage Society but copies have been used in business classes at Stanford Business

School, where it's become the basis for entrepreneurial lectures. So, I have that document if you ever want to see it.

SHINDELL: Well, actually, Howard made me a copy of it.

ROYSTON: Okay.

SHINDELL: I think I have a copy. And actually, Ted Greene also told me about . . .

ROYSTON: It's now . . .

SHINDELL: Told me about the case study there.

ROYSTON: Yeah.

SHINDELL: Yeah.

ROYSTON: I Ted and I did the case study at Stanford, it became a case study up at Stanford Business School, and this five-page document that I wrote, "Dear Brook," it's a five-page letter and I outlined the technology, why it was important, the competition – there wasn't any except for one small thing – and the funny thing is I said, "What would we do with these antibodies to make money?" And, so I realized, well the immediate thing was blood testing. Because, when I thought, "What's the most important application for antibodies in 1978?" Well, the hepatitis blood test, which every unit of blood was screened against, was done with an antibody test, and they were using these impure antibodies that, extracted from serum of rabbits, or whatever, and I said, "We could make a much better test if you had a monoclonal antibody to hepatitis." And then, obviously the opportunity to make antibodies to many other agents. And, because most, many tests were antibody-based. So, I wrote that up as, you know, "We could make this diagnostics business and then maybe in the future, you know, we could work towards making antibodies as therapeutics," but that, of course that's, it takes a lot of, a longer term. I sent that, that letter to Brook Byers. It is now well documented. As I say, it appears in a number of places, as you know, and he hired a due diligent expert, another scientist in the antibody space to read it and I guess it came back positive. And, the bottom line is, by September or so the whole team of Kleiner Perkins Caufield & Byers flew down to San Diego to our lab and met with Howard and me and we spent the whole day with them. We showed them how we made the antibodies, how we made the cell lines. We showed

them the cells under the microscope, and then we showed how we tested for the antibodies. And, that afternoon they asked me, after driving them to the airport, and I think I was alone. That's right. Howard wasn't with me. And, we're at the airport and Tom Perkins, who's really famous today. I don't know if you know him. You know, he owns the Maltese Falcon, the boat, and he was married to Danielle Steele. So, Tom Perkins says to me. "So, Ivor, how much money do you need to show me that you can make these antibodies outside the university? You know, you open up a lab somewhere else." So, I said, "Well, you know, we can do this for about," I said, "a couple hundred thousand dollars. Give me a couple hundred thousand dollars and we can make some antibodies for you." And then Tom looks at me and says, "I'll give you $300,000 and we'll take," I think he said, "We'll take sixty-five percent of the company. We'll form a company. I'll take, we'll take sixty-five percent. We'll give you $300,000 and you and Howard, and all the future employees of the company will split up the other thirty-five percent." [Laughter] So, I said, "Fine." You know, that somebody was going to support us to start a company, that's all we cared about. We didn't know anything else. The biggest question I get at Stanford Business School, when I give the lecture, is, you know, "Why would you sell so cheaply?" Well, making money wasn't our primary objective. We weren't there to make money - I was trying to figure out how to cure cancer in those days. So, they gave us $300,000, and Howard will tell you stories about what he did with the check and how his car broke down [Laugh] and all that kind of stuff. Neither of us had ever seen that much money. I come from a lower-middle class family. We had never seen a check for $300,000 before. But, you know, they just wrote out a check. And, "Here's the money. Go put it in the bank." So, Howard was in charge. Well, I had made arrangement, at that point when they agreed to fund the company Howard agreed to leave my lab at the university and help set up the company, and build it because I, I was still a faculty member. He was a laboratory technician. So, he agreed to be the first employee and then he went out and he did a great job, because he then hired this really great scientist from Scripps to come and join him. And, and so the goal was, to prove to us that you can make an antibody outside the university." And, we had said, "Well, what antibody are we going to make?" So, I said, "Let's make hepatitis antibodies," you know. "Why not? It's the number one test being, I mean, that's being used for antibodies." So, that's what we did. So, we got a hold of hepatitis antigen and we started injecting mice with it and, and that was all done outside in a private laboratory. But, here's the interesting thing. So, the company, Hybritech, had formed. They needed the cell line. This is something that would

never happen today. I took the cells out of my lab at the university and gave them to Howard and he took them over to the company, and that was – because the company had to have the cell line to have, to start to make the antibodies, like yeast.

SHINDELL: It was that, that simple? Just move them over?

ROYSTON: That, it was that simple. It could not be done today. [Laugh] You can't move biological products that have commercial value from one university or, in one entity to another without all kinds of agreements. But in those days, it was the Wild Frontier, there were no, there was no biotech industry, and there were no agreements, and no one even thought about implementing what we call an MTA, a Material Transfer Agreement, which came later, in the '80s, after people saw what happened. [Laugh] So, I took the cell line. And, no one's ever accused me of – we don't even know whose, who owned those cell lines. I mean, I got them from Stanford, and the guy from Stanford got them from Cambridge, and the guys in Cambridge never patented the technology, and they've been harshly criticized for that. The MRC in the UK lost hundreds and millions of dollars because the technology was never patented. Because scientists didn't think about patents. Here was one of the most important discoveries ever made in England and it was never patented. Can you believe it? The Cohen-Boyer group in Stanford and UCSF patented the genetic engineering technology and they got a tremendous amount of royalties from all the genetic engineering companies, Genentech, Amgen, and so forth, and every company that was doing genetic engineering. But, in the monoclonal antibody space there were no patents, and that's why I was able to do what I did. But, the company got off the ground because the cells that I brought down in my tank from Stanford [Laugh] to San Diego then made its way over to the company. The company gave birth in the labs of the La Jolla Cancer Research Foundation that had some additional space they were willing to lease to us. And so, Howard was in charge, hired the guys, and Brook Byers became acting president. He flew down here every week, spent a couple days, a few days. I was acting chief scientist and I did that after hours, and Hybritech gave birth, and then within, again, I guess we had the magic touch in those days, within three to four months we had antibody, we had pure monoclonal antibodies to hepatitis, all kinds of different subsets of hepatitis virus. So, we accomplished our goal, the milestone. Kleiner Perkins, the firm, was very pleased and they pumped in even more money into the company. At that point, the next stage was they put in maybe, I can't remember if

it's the stage they put in $5 million maybe, or a million, or $2 million. I mean, in the millions. But then it came time, now that they saw this could really, this is for real, that we could reproduce what we did that it was time to get a permanent CEO, and that's where Ted Greene came. So, when we heard, Brook and I, that there was this guy named Ted Greene, who was ex-Baxter executive, who a year after us had decided, "Well, maybe there was a future in the monoclonal antibody arena," and was going to put together a team to develop a monoclonal antibody company, well Brook and I said, " let's go talk to him because we need a CEO. Maybe all we have to do is convince him to be our CEO and then he'll drop his plans of trying to create a company that would actually compete with us." And that's exactly what we did and I think both Howard and I will remember the day when we drove up to Newport Beach where Ted Greene lived and got together with him with Brook Byers and we suggested to him, "Look, we're already up and running. We've got, we've already made hepatitis antibodies with this, you know. We've got Kleiner Perkins, the number one venture capital firm behind us that started Genentech. Let's go – why don't you join us as the CEO?' And after all the protracted going back and forth he did that. He joined us as CEO.

SHINDELL: How did you all know that he was interested in monoclonals, because according to him he was trying to keep that . . .

ROYSTON: Have you already done the Ted Greene interview?

SHINDELL: Yeah. He was trying to keep that information sort of secret.

ROYSTON: But it got out.

SHINDELL: It got out? Okay.

ROYSTON: This is a small world, right? I mean, people, I don't know who heard about it first but probably I think – no, Brook Byers heard about it first.

SHINDELL: Oh, okay.

ROYSTON: So, Ted joined us as CEO and you know what makes a successful company is not just the technology or what I did or, it's bringing in the right managers. And, I'm a firm believer that you can't have a successful company without the, the best managers, like Ted Greene. Because, what it, you know what Ted did?

The first thing he did when he came in as CEO, and this is very important, is he, when he saw what we had, you know, we had the technology up and running, we could make antibodies, and we had, and we had hepatitis antibody so I, you know, I was pretty naïve. I'm just an academician. I said, "Okay, well we ought to compete with Abbott that had the monopoly on hepatitis tests. Let's compete with Abbott and we can come up with a better hepatitis test, you know." And, Ted Greene looks at me and he said, "Are you crazy? You don't go, you don't take your first product that you're going to bet the company on and go against Abbott. They're going to destroy you. Abbott is not going to give up their testing that easily and they'll destroy you." And he said, "We are not going to develop hepatitis testing. You," he says, he said to us and we now had a bunch of scientists there, he said, "You guys have got to come up with another product that we can develop as a lead product here, in the diagnostic space, because the therapeutic area of treating cancer that's, that's years and years away." But the idea that Ted, and we all agreed with that Ted came up with, "Let's come up with a diagnostic strategy that can bring in near-term revenues because, you know, you don't need FDA approval for that." You just – well, you do to sell a diagnostic test you need to do some studies, but it's not like therapeutics. "Let's come up with a diagnostic test that we can sell to them, you know, based on these monoclonal antibodies to bring in near-term revenues while we build our therapeutic program." And so, we're sitting around and I'm still acting, chief scientist, and I can remember the day we were sitting around with our little group around the tables, "What are we going to work on? What are we going to work on if we're not going to do hepatitis?" And one of the new people, it was Gary David, and you can certainly interview him. He was one of the, first scientists there. He said, "You know, I've been reading about this new antigen called PSA, and it was discovered or developed, discovered and characterized in Roswell Park, and they claimed that it secreted in patients with prostate cancer and it might be a market for prostate cancer. Why don't we make an antibody to that and develop a test for prostate cancer? Maybe we could develop and early blood, early diagnostic test for men to pick up prostate cancer while it's still early?" We all said, "Hey, that's a great idea. Let's get some more information." And actually, that's what happened. The company said, 'Yeah, this is a great opportunity. That's an untapped market." There was some interesting evidence that maybe that measuring PSA levels in the blood might tell you whether a man might have early-stage prostate cancer. So, we decided that's something we ought to explore. And so, somebody in the company went ahead and made a deal with Roswell Park to license in that antigen. So we injected it into,

this PSA antigen that was discovered, injected it into mice, made the antibodies, developed tests, and sure enough – I'm jumping years now, several, a couple years – we were able to demonstrate in that we could pick up prostate cancer, and the PSA test ultimately became the most important new development in prostate cancer, because all men over age fifty get the PSA test today, and I just got mine last week, for prostate cancer, picking up early, a lot of men have been diagnosed with prostate cancer because of that blood test. And, that's another long story about whether that's useful or not, but it's a very, very common test today and that was developed by Hybritech by our team. So, of all the things that Hybritech ultimately did contribute to society, was the development of that test. They did make other tests as well, pregnancy tests, CEA test for colon cancer, but the most important test for society, was the PSA test for prostate cancer. Interestingly, Abbott laboratories ultimately developed their own. Because, they were the number one diagnostics test maker in those days. So, here's a great example of how having somebody out of industry who understood, strategically, that you don't bet your first product and compete against a giant in the field but go after something new paid off. Hybritech went public in 1981 and by, and then, at $11 a share, when there was a public market, you see, for it, and then by 1982 did another public offering at $22 a share, and ultimately was acquired by Eli Lilly. And that story relates to the fact that, that even though we had this diagnostics business we knew that long-term the real value for the company lay in developing therapeutics, but we also realized that it would take a lot of money. And, I remember Tom Perkins coming in one day and, he was on the board, and said, "What if I could get you a pharmaceutical, a pharmaceutical company to come in, acquire the company, but at least, and leave you guys to be sort of semi-independent to continue the work but you'd have all that money from the pharmaceutical?" And, that led to the acquisition by Eli Lilly, which took place in 1984 or five. And that's what happened. We were acquired by Eli Lilly.

Okay, so I've just described for you what I consider the, you know, the birth of the industry, because Hybritech was the first biotech company in San Diego. Now, me personally, I want you to understand that, oh, I, even though initially I was the chief scientific officer by, so once Ted Greene was there he wanted to hire a permanent chief scientist to do it. So, he hired a guy named Tom Adams. He came out, after a year of negotiations, so he probably came in about 1980 or so, or something like that, and came on board. And so, my role now was really one of being a consultant to the company and being on the Board of Directors, and I was focused, you know, I was

still focused on my academic pursuits of, of using antibodies for treating cancer. And, and but working with Hybritech was helping me to some extent in that. So, so one, just on a sidelight then you need, one thing that's – it's interesting you're doing this for UCSD Library. But, you ought to know that in those days the idea that one of the faculty members would be involved with a company was not, not mainstream. It was actually looked down upon, to some extent. People started asking questions about my involvement with Hybritech. They asked "Well, how can he do that? How can he be a full-time member of the UCSD faculty and at the same time start a company?" Well, the fact of the matter, and it all goes, the answer to that is because of the twenty percent rule that all faculties have around the country and university is that you're allowed to use twenty percent of your time to consult for other companies, and there was no prohibition to getting stock, or fees.

SHINDELL: Now, is, was your perception that they were upset over the additional income or was it maybe this sort of image of, like, isolated ivory-tower science being maybe corrupted by working outside as well? Sort of breaking down that wall between academia and industry?

ROYSTON: This ivory-tower concept was already breaking down because there was this class distinction between what we call "basic scientists" and "clinical scientists." I was always considered not a basic scientist but a translational scientist, so I always felt that the basic scientist, the ivory-tower basic scientist who do pure science always looked down upon me. And, that's a whole other story, because there was also, at UCSD in those days, you had the basic scientists on campus in La Jolla and you had the clinical scientists downtown. We were even separated. No, it was much more, "Wait a minute. Ivor started a company and he's got all this stuff? How could he do that and still be on the faculty? How did he do that? Is that legal?" you know. [Laugh] Well, the answer is yes, it's legal. Yes it's, there is the twenty-percent rule, that a faculty member could consult for other companies twenty, up to twenty percent of his time. So, on a legal basis, what I was doing was I was consulting for Hybritech up to twenty percent of my time. So, there were no problem there. And, there were no rules that said that I couldn't have stock in the company. Or even if I spent time over at Hybritech I was allowed to do that, up to twenty percent of my time. And, any professor was allowed to consult for a pharmaceutical company or, any professor could consult for any company and that was a way, of course, to allow academics who had modest salaries, to boost their income by getting consulting fees.

In my case, it wasn't so much the cash fees it was the equity that I got in the company that I was consulting for. But, what happened is, there were a lot of secret meetings taking place at UCSD amongst the faculty. Like, "What do we do with Royston?" -

SHINDELL: Really?

ROYSTON: - "How can he do this? There must be something wrong." And those were the days when people looked, look down on commercial involvement. And they were, I mean, yeah a little bit, somewhat an ivory-tower mentality, but looking down on people, who were spending the time outside and benefiting from it. Of course, it wasn't really any different from any faculty member in any department who, who consulted for any company. But, this was different.

SHINDELL: Well maybe the – is it because the life sciences sort of were, you know, they didn't really have a tradition of that?

ROYSTON: That's right. There was no – it was not like the engineering school. There was no tradition in life science, and you're absolutely right because all you have to do is look at where we are today. Today you're the exception in medical school if you're not consulting with somebody or not a founder of a company. Things over the past thirty years, have changed dramatically. I was there on the front line - in the beginning. So, as Brook Byers said, the famous quote when I complained to him about this situation, he said that, that "Herb Boyer, the founder of Genentech, went through the same thing, to some extent," And, he was a professor at UCSF. Brook Byers's comment was, "Well, don't forget Ivor, pioneers always have arrows shot at them." [Laugh] And, and that's the answer to this dilemma. So, he was saying, "Look, you're the pioneer down here in San Diego. You're the first. You're going to have arrows shot at you," and that's what happened. I mean, it did also lead to, at one point, anonymous letters being sent in to NIH asking them to investigate me because they just figured I was doing something wrong. And, they did do an investigation. They didn't find anything wrong. But, I always tried to be absolutely scrupulous about things. But, but I was investigated. And, these are the kinds of things that you had to put after, but now years later this is the norm now. So, I paved the way for all those that came later. I had to take some hits, but they were just emotional ones, people not wanting to talk to me in the hallway, things like that.

SHINDELL: Did you ever question what you were doing -

ROYSTON: No.

SHINDELL: - at this time? No?

ROYSTON: I always felt that what I was doing was right. But remember, my goal all the time was, "How do I get this stuff into patients? How do I treat patients?" I was not in it for the money. I didn't start Hybritech, "Oh, I've got this great technology. I want to make a million dollars." No. It was, "We've got to start this company so I can make the antibodies so I can get them into patients so I can test them to see if these antibodies will be a new treatment for cancer." That's what it was all about. So, but now over the years developed, having worked with people like Brook Byers and other business, and venture capitalists and understanding their business more and developing a respect for what they did, ultimately I think when you get older and maybe you realize that you're not going to be getting the Nobel Prize, like Roger Tsien just got at UCSD,. someone like me would rather work as a venture capitalist helping other creative scientists be successful , I decided to start, I decided to move in that direction and to become a venture capitalist, which I started that process in 1990 but it didn't complete until about 2000 when I came here full-time. And even though I started this company with Stan Fleming, and I had voluntarily left UCSD to become the head of the Sidney Kimmel Cancer Center, which I did until 2000.

Biogen Idec was an outgrowth from Hybritech. Once Hybritech was sold to Eli Lilly and I was still on my quest to use antibodies for treating cancer, I decided it was time to, to focus on a company that was really focused on treating cancer with antibodies, and I was able to convince Kleiner Perkins and Venrock, another firm, to fund IDEC for the purpose of making monoclonal antibodies for treating lymphoma, cancer of the lymph system. And, and that was successful. And, the first antibody for cancer was Rituxan, which was approved by the FDA in 1997, even though we formed IDEC in 1985, about the time that Lilly was acquired. The same time that Lilly acquired Hybritech is when I formed IDEC. And, and IDEC became a very successful company here in San Diego.

SHINDELL: Uhm-hmm. You worked with Bill Rastetter there, is that right?

ROYSTON: Yeah. So, Bill Rastetter became the CEO. So, again, I teamed up with Brook Byers and then again for the second company, and then we needed to hire a CEO so we, it was Brook again that had heard that there was this really top-notch guy at Genentech, named Bill Rastetter, that may, maybe would be a good candidate to be CEO of the new company. So, we interviewed Bill and then he got the job. Yeah. And, he became the CEO of IDEC.

SHINDELL: This isn't exactly a historical question but, you know, if you could take the you of today and stand next to the you of, you know, the early days of Hybritech, you know, do you think that your mentality now as a venture capitalist verses, you know, a scientific advisor or chief scientist, has that mentality changed? Would you have different ideas now, the person you are now versus who you were then? Is there a difference between a chief scientist and a venture capitalist?

ROYSTON: Well, my chief scientist in a company or . . .

SHINDELL: Well . . .

ROYSTON: what I was back then was still an academic scientist.

SHINDELL: Right.

ROYSTON: I never was an employee in industry. I was an academic scientist trying, publishing papers, trying to discover new things, and particularly trying to develop new treatments for cancer using antibodies. That was my role at the university. I was a full-time university faculty member. My goal was to cure cancer.

SHINDELL: So, I'm wondering if . . .

ROYSTON: So, if you say, my "you" of back then, me back then was focused on my science at UCSD. The Hybritech, or the IDEC, those were like sidelights for me. They were not my major goals. But, ultimately I, as I said I developed an appreciation for that, and over time I realized that the convergence of business and medicine was an, a way to accelerate discovery and to accelerate getting ideas into the clinic and into the market place for the benefit of people. But an overarching goal as a venture capitalist is to make a good financial return for our investors. The two goals are really very different.

SHINDELL: I think that's what I was . . .

ROYSTON: As a university researcher I realized, "Boy, you know, you write all these grants to do your science. You have to really love the science to do that, you know, building, doing small incremental studies to build on the science. It's a building block thing. And, and you write grants, and you get, you know, $100,000, $200,000 a year for your work, and so forth. But, there was something about being able to take millions of investment dollars and focusing it on somebody's science, where there might be some great innovation, and really creating something from nothing and moving, and developing a whole new technology or product area, like I had done with Hybritech and IDEC. But, at some, and so as I grew older I realized that the skill set that I had developed might be useful for others, so that I could play a role with the next Ivor Royston, you know, down the line, or the next person who had a great idea. And with my experience I thought, once you realize that you're not going to get the Nobel Prize yourself, that you're not going to, that all you're going to do is – at one, if you believe that you're not going to make that big discovery that's going to really change the world [Laugh] then I felt that what I could do, I could play a better, a better role at doing, or at making a major contribution by combining business and medicine. The combination, the joining of business and medicine is a way to really accelerate discovery and move things along much faster, and I could see that from my own personal experience and I decided that, that that would be something that I would like to do. So, I moved in that direction over time to where I am today, which is what I do today, here at Forward Ventures.

I teamed up with Stan Fleming. So, when I was running the Sidney Kimmel Cancer Center I decided to leave the university because of all the bureaucracy and I wasn't as concerned about long-term tenure, and I had the successes in Hybritech and IDEC. And, I decided that the opportunity to build my own cancer center, with the help of other people, and it turned out to be Sidney Kimmel, I was able to get to know Sidney Kimmel quite well, who's, was the owner of Jones New York, and made a major commitment to cancer research. So, we started the Sidney Kimmel Cancer Center in San Diego and we built that up very nicely. And, and at the same time I dabbled with getting involved with venture capital with my own money, and Stan Fleming joined me, and he said, "Let's build a real venture capital firm. I'll be the business guy, "I'll do the work." And so, we did build a firm to where it is today. And then at, and then, back, as both this cancer center and Sidney and Forward Ventures

were growing it became clear to me that I had to choose. And then it also became clear to me that choosing Forward Ventures is how I wanted to finish up my career because I evolved at the Sidney Kimmel Cancer Center as more of an administrator adjudicating fights between professors, or its faculty members who wanted more space and more money, and I really wasn't, I didn't feel like I was really moving the ball very far in the nonprofit area. I decided to pursue the venture capital model with Stan and spend full-time on venture capital, which I did starting in 2000. So, I've been full-time here at Forward Venture since 2000, so eight years, but, and part-time since 1993 when Stan joined me to start the institutional Forward Ventures while I was still running the Cancer Center.

SHINDELL: Uhm-hmm. Now, I have a whole other set of questions that's really more to do with the sort of the landscape of San Diego biotech and what you've witnessed, you know, as the landscape has changed, or -

ROYSTON: Dramatically.

SHINDELL: - as this situation of biotech startups has changed over the years? But, I know that you wanted to keep it under an hour, so maybe we can leave that for a follow-up (Royston: Yeah.) interview, if you'd like?

ROYSTON: Sure.

SHINDELL: Okay.

ROYSTON: I do, just to make a comment, that the landscape has obviously changed in the quarter of a century. You know, when I, when I started Hybritech there were no biotech companies here. There were no service providers, there was no nothing here. Everything came down from the Bay Area. Now, you have one of the top regions in the world for biotech. So, I'm really happy that I played some role in that. You know, I mean part of the first company. But, all those people – and, you know, it's a fantastic community and now we're in an environment where, where most medical scientists and professors enjoy being involved with biotech companies, and pharmaceutical, and it's an active effort by all of the university administrators and program leaders to develop ties with industry, and the biotech community. So, everything's totally flip-flopped over the years. So, I feel like that's great. And, people understand the importance of the industry. The other thing is we went through an

era in, in the '80s where NIH money declined abruptly and people were scrambling for grants. We actually are in one of those eras right now, and because, and there were opportunities within the biotech industry, companies that had started to, to actually give out grants and so forth, and people understood that there might be opportunities to get money for their research, when there's more biotech activity. So, yeah, things have changed dramatically, and we can talk about that next time we meet. And, that'll be good.

SHINDELL: All right. Great. Well, thank you very much for putting aside this time.

ROYSTON: Yeah. You can just schedule a time . . .

END OF 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.