Ivor Royston

Interview conducted by

Mark Jones, PhD

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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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INTERVIEWEE: **Ivor Royston**

INTERVIEWER: **Mark Jones, PhD**

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JONES: Let's start from the beginning.

ROYSTON: I came from very humble beginnings. OK, I was born in England, 1945. My father was a sheet metal mechanic. The reason I was born in England was that my mother and father met in England during the war, World War II. And both of them had come from Eastern Europe, separate countries. My father was from Poland, and my mother was from Czechoslovakia, and because of the war -- we were Jewish -- they found themselves in England, where they got married. My mother, the reason she explained why a Czech married a Pole was because it was wartime, and I guess that didn't happen outside of wartime. My father had fought in several armies, starting with the Polish Army, and then the French Army, and the British Army, and all that -- but that's a whole other story, which is fascinating. But my mother had left Czechoslovakia before the war broke out, and just never went back. She went to visit England before 1936, when Czechoslovakia was invaded, and after it was invade by the Germans, she just never went back. So, my mother never saw her family again. My father was in the Polish Army when Poland was invaded, so he fought in the war, and then via Dunkirk, the evacuation of Dunkirk, made his way over to England. So, anyway, I was born in England to parents that had no relatives in England, and after the war, they began raising their family. And as I said, we were what I would say, a low-income family, my father had a trade, he never had a college education because of the war, he was college age when the war broke out, eighteen, nineteen, something like that. And he had a son to support, because when he came back from the army, the British Army, he was part of the Berlin occupation force, and when he came back, he had a two year old son to deal with, and he had to raise a family. Now,

I had an uncle who lived in the United States. My father had one living brother who also escaped Poland during the war, and made his over to the United States, and over a nine-year period, convinced my father to eventually emigrate to the United States. So, in 1954, my parents moved from England to the United States. And by then, I had two younger brothers. I had a brother who five years younger, and another six years younger. So, when I was nine and half years old, we took a boat to the United States. My parents just packed up all their belongings and moved to the United States. My uncle sponsored us, found us an apartment to stay in, in New Jersey, Plainfield, New Jersey. And, there my father worked and in a year, I lost my British accent, because I was at an impressionable age, and he eventually got a job in the Washington, D.C. area, a year after. So, a year after, we moved to Washington, D.C., and that's where I lived until I went to college. I went to grade school, junior high school, and high school in Washington, D.C.

JONES: Were you a good student?

ROYSTON: Yeah, I was a good student, I guess I was more As than Bs, primarily As, with an occasional B here and there, and I was always doing well in mathematics and science, and then occasional Bs in English, liberal arts. So, I excelled in math and science. My father had a job as sheet metal mechanic. By the way, in England, he did a lot of roofing work, too, so one time, the company that he worked for was asked to reroof one of the famous castles in England, Heever Castle formerly owned by King Henry VIII, where Anne Boleyn lived. And he took us there for the summer and we lived there in the castle while he did the roofs, so you know, that was a lot of fun. So, there were some benefits to being the son of a roofer. That was a fascinating experience. And he was involved with the roof on Royal Festival Hall, which was built in the early fifties for the coronation of Queen Elizabeth. So anyway, in the United States, he also became a sheet metal mechanic, and there was less roofing, perhaps than other metal work. Whatever metal work that needed to be done at the construction company, whether it was gutters or partitions, that's what sheet metal mechanics did. He learned that trade from his uncle when he was in Poland, that was what he decided to pick up on. I finished high school at Calvin Coolidge High School in Washington, D.C. As far as that impacted my future career, well, first I was co-editor of the yearbook in high school. I didn't have that many extracurricular activities, but it was during high school that I had my first experience with research. I got a summer job at Walter Reed Army Hospital through a National Science

Foundation program that supported summer students. I was really interested in science, and I applied for it, and I got it, and it was really very enjoyable for me to be there in the hospital, working as a student, and I'm sure it had something to do with propelling me to continue because I really enjoyed it. I enjoyed doing research, interacting with doctors and scientists. And that's why I do that here. Running this institute here, I've been trying to tell the staff that I really would like to have high school students come and join us here for the summer because I know what it did for me. The other major impact, and this is where it relates to the business side, is it was in high school that I was exposed to business in a very important way. And I can share with you, if you want to see some primary materials, a business organization that I was a part of called the Chessmen. In high school, this is Calvin Coolidge High School in Washington, D.C., I had a classmate whose father was the vice-president of a bank, and his father decided that he would like to give his son and his friends an educational experience in business. So, he got my friend to get his friends together to start a little investment club, and it turned out to be sixteen of us, and I coined the name 'Chessmen,' because of the sixteen pieces. And they adopted that name, so all of us got together and called ourselves the 'Chessmen.' Now, eventually, the Chessmen actually did reasonably well in our investment portfolio, and it was written up in the Washington Post, a full page article on the Chessmen, and have that -- it's pretty wrinkly right now -- I was in high school from 1960 to '63, so over thirty years ago. And by the way, there was a speech I gave when I received an award, and I brought this article, and there was some write up here in the San Diego Union about it. The Chessmen focused initially on investing in second trust notes, buying second trust mortgages. See, you buy them at a discount, and as the thing matures, you would get monthly interest payments, and then you would get the full value of the note. So, as kids, we used to go out, we would look in the newspaper for second trust mortgages that were for sale, and then someone would go out and look at the house and give a report to the group and say, you know, 'this is a really good home, well-built, and these people have been paying their mortgage on time for the past ten years, and it's really very safe,' and so forth and so on, and we would actually go ahead and invest money in these mortgages. And what I did was to put my allowance money in there, and I got my father to provide some money for me, but anyway, I basically invested my money, whatever my savings were. And over the next two or three years in high school, the value of our investments did go up significantly, so we actually started making money, and it was doing quite well, until the very end, when we started going beyond our reach. We all took a limited

partnership interest in a major high-rise development project, and that did not do as well, so in the end, the developer had some financial problems, and in the end we probably lost some money, so it did not have a positive outcome at the very end. But during this whole period in high school, I was exposed to business and investing, at an early age. And that was a very positive experience. It was a lot of fun. Even though I was very interested in science, I was also very interested in, and thinking about, business things. So, when you look at what's going on today, and you look back to my early life to try to find these parallels, you'll find it there at the very beginning. My father had no real business experience, he was a tradesman, there was no doctor in the family, no scientist in the family. I had very few relatives anywhere, so there were no role models.

JONES: What were your parents' expectations for you?

ROYSTON: Yeah, well, my parents lived for the children, they worked hard, my mother got a job, my father worked hard, and all of the money went into our education. We did eventually -- I was in private school until high school, and they worked for the tuition, and then for college, well, I got loans and scholarships, but they made it -- as long as we were doing well in school and studying hard, they pretty much did everything they could to accommodate us.

JONES: And the expectation was that you would go to college?

ROYSTON: Yes, they wanted us to succeed, yeah, and to have the life that they didn't have. That was a very important driving force, I imagine. I mean, I look at my children today wondering whether or not they're going to have the same kind of drive that I have. I have two children, a sixteen year-old daughter and a twelve year-old son; I think my son does and my daughter doesn't so much, so I don't know, we'll have to see. But I was pretty driven. My parents made it easy for us to get our work done. They didn't overload us with chores, and we didn't have to go out and earn a lot of money. They basically put their savings into their children's education. They lived for their children, essentially. Education was very important. So their expectations were that we would go to college and probably be in some profession. No one asked me to go into medicine, they were certainly very supportive of me becoming a doctor. For them, it was going to be a real honor to have a child become a doctor. My middle brother's a doctor, too, so they had two doctors in the family. We all went to college. My youngest brother went to college and got a degree in

business administration, and is a budget analyst for the Secretary of Agriculture in Washington. But my middle brother is a physician in Atlanta right now, so we have two doctors in the family. My parents were happy that I had chosen medicine as a career, but there was no pressure on me by anybody to go into medicine, and in fact, the idea of going into medicine or medical research did come up, or come to me, pretty early on. I mean, even before high school, I started to focus on medicine. I used to go to the library and read medical books. I got fascinated with how the body works, and I don't know, it wasn't too long before I got focused on cancer. Cancer research is the area of interest for me.

JONES: So even after the investment club, it was clear that medicine was going to be your career of choice?

ROYSTON: I was really much more driven toward science and medicine, than investment -- but it comes back; I'll give you some other influences. After I graduated from high school, I applied to various colleges. I was accepted at a number of colleges, but for financial reasons -- one of the places where I got a scholarship was the University of Pennsylvania. I was only going to go to a place that offered a scholarship because of our financial situation. My parents could not afford a major college bill at that time. But then, for some reason, I decided to make it easy on myself, maybe part of it was not wanting to leave at that time. It's interesting, because later in life I decided that I wanted to get as far away from my parents as possible, but early on, I decided to stay in Washington. I went to George Washington University for a couple of years. But then, as soon as I was there, I started applying to other schools. I applied to Johns Hopkins University. I did well at George Washington; I got mostly As except maybe some Bs in English. English was hard for me -- English composition, things like that. I think the English composition teacher is now a Provost at UCSD -- Lyon. Isn't there a guy named Lyon at UCSD? He must have retired by now. I think he was the same guy. I remember he was really tough on my English composition. So anyway, I applied to Johns Hopkins University. Now keep in mind, while I was at George Washington University, I continued to do summer jobs in research institutes. For example, after I had had my Walter Reed Army Hospital experience in high school, my first or second year in college, I applied for a summer job, and got one, at the agricultural research center in Belsford, Maryland, where I worked on plant viruses. This was my first year in college as I recall. And I kept building on my experience, so by the time I applied to Johns

Hopkins University, I decided to apply for a special program called the 2-5 program. You're accepted after two years of college, you get your bachelor's degree at Johns Hopkins, and you automatically go on for your medical degree. And the first year in the 2-5 program would be to spend your third year of college on the college campus in Baltimore, the Homewood campus, to emphasize liberal arts, because there's no pressure on trying to get into medical school -- you're already in medical school -- you could spend that last year really taking the course you wanted to take. So, I applied for that, and I got in. I think I got in primarily because I had good grades, but also because they could see from my summer job experience that I really had a commitment to research. I told them I wanted to medical research, and Johns Hopkins, like Harvard and other places like that, prided themselves on turning out academic investigators, medical researchers. So, I was accepted into this special program; they only took about twenty kids, twenty students, and that's exactly what I did. In the next year of college, which was the first year at Johns Hopkins, my third year of college, I was in the Homewood campus, where I took all kinds of liberal arts courses. I didn't worry about the grades, it didn't matter anymore. Whereas at George Washington, I was taking things like abstract algebra, which had nothing to with medicine, just because I did well at it. I liked to challenge myself at mathematics. I scored tenth in the city of Washington in the mathematics high school contest. I was in the top ten, so I was strong in mathematics. I took some things like, some really excellent political science courses, I did take a meteorology course, a weather course, and one thing I regret is never taking an economics course. I took sociology, I took anthropology, I took a lot of stuff like that. Then, I finished medical school at John Hopkins. In 1970, I graduated with a medical degree from Johns Hopkins, I had a bachelor's degree also from Johns Hopkins. And I continued to work in the summers, like the first year I was at Johns Hopkins [med school], I also then got a job at the National Cancer Institute in Bethesda, which was close to home. So all of that continued to build on that experience. Now, while I was at Johns Hopkins Medical School, to go back to some things that impacted my business side, I married for the first time, I've been married once before, I'm married to my second wife now, who's downstairs, the one that introduced me to Brook Byers. My current wife I've been married to since 1978, it will be twenty years next year, nineteen Years this month, our anniversary is this month. But I was married before her six years to a woman that I married while I was at Johns Hopkins Medical School. And six with her, no children, but her father was a very successful businessman. So my first father-in-law was an extremely successful businessman. He had, you know, a net

worth of many millions of dollars. And his business was primarily real estate. He owned high-rise buildings in the city center, the city of Philadelphia, and had real estate projects all over -- Washington, D.C., Europe -- so he was a very successful businessman. And he was also a real...very, very quick, very intelligent, very high intellect person when it came to mathematics and business things. He was constantly, every time I'd meet him, he try to challenge me, you know, to solve problems, business problems, and things like that, and if I didn't do well at it, he'd tell me how stupid I was, or something like that. He was a pretty arrogant guy, too. Now I don't know how much of a positive influence he was on me in terms of getting involved with business people. I certainly wasn't afraid to get involved with them, because if I could deal with him, I could deal with anybody, you see, but certainly through that six years of experience of him being my father-in-law, I certainly had the opportunity to relate to a successful businessman, and to see the positives, and some of the negatives, because I saw how he treated certain people in business and I didn't appreciate it, didn't like it. I think that, through these associations, though, I sort of just naturally learned, and a lot of things in business just came easily. I understood it. I mean, I wasn't afraid of business or thinking about business. It seemed to be part of my life. So after I graduated from Johns Hopkins, I moved to Stanford University to do all of my post-doctoral work, in 1970. So, I moved to Stanford. In my first two years at Stanford, I hadn't met Howard yet. I was doing my internship and residency in internal medicine. And I was there with my first wife. Her name was Anita. And then, I went back to the NIH in Bethesda, Maryland to work for three years. Initially it was going to be two, and I extended it a year to three years, to do research there in lieu of serving in the military. 1970 was the last year of the draft, so as a physician- researcher, I had the option of signing up voluntarily with the Public Health Service to do research, if I were selected, that is, in lieu of possibly being drafted into the army. I was selected, again because of my research background, the fact that I'd done research throughout my summers. I'd been at the National Cancer Institute and had done pretty good work. The fact that I was at Johns Hopkins, all those things, allowed me to be selected to the Public Health position. It was a very competitive thing. So, I was offered a position at the NIH in the Public Health Service, in lieu of the military, and I did that tour of duty from 1972 to 1975.

JONES: And this was the first time you'd done your own independent research, or had you been doing your own projects before?

ROYSTON: Oh, that's a good question. One of the things that I didn't mention was that at Johns Hopkins Medical School, you get one quarter elective every year you're at medical school, so it's three quarters of required work, one quarter elective, but a few people, and I was one of them, chose to do all required work consecutively for three years, so that the final year became all elective. So, in other words, I got all my course work done in three years, because if you take a quarter out from each year that makes a year. I opted to do a year elective, and I did it in the laboratory, I did research in the microbiology department, working with viruses and cancer. My project was to work on the association of herpes simplex virus and cervical cancer. So, I looked to see if there was evidence that in cervical cancer cells, there was evidence that herpes virus was in any way involved with the cancer, by looking for viral products.

JONES: Did you find any?

ROYSTON: Yeah, and we published it, and that wasn't my first publication, but -- my early publications were published while I was in medical school -- so I had already started having a literature -- a publication record. My first paper was my first year at Hopkins, actually I went to Israel and did research there, and that led to a publication. It was more epidemiological.

JONES: How did you end up at Stanford?

ROYSTON: I applied there, and it was my first or second choice. After finishing medical school, you apply for internships, and you rank order the places you want to go to, and then the hospitals rank all the candidates and a computer matches you up. I decided to go out West, and that was my first time out west, and that was what brought me here. I had never been west of Washington before.

JONES: So, because Stanford was a good place, because it was out West, and...

ROYSTON: And because it was known for its work in cancer research, oncology. So I interviewed well there, and I was accepted there. I may have ranked UCSF number one, and Stanford number two, but anyway, I was happy to be at Stanford. Going out to Stanford, having been in Baltimore, it didn't really look like a hospital to me, but anyway, I was there two years, and then I went back to NIH to fulfill my public health service duty, and there I did independent research. By that time, I was now

ready to do independent research, so even though I had a sponsor, I really had my own lab, actually, and technicians, and I started doing my own independent research and my project was to work on what caused mononucleosis. It was quite productive. From our little group, there was another guy just like me, now at USC, and he worked on one aspect, and I worked on the other aspect, and we were able to elucidate what was going on in infectious mono, so that led to my first major New England Journal publication back in 1975, I guess it came out. And then, after the three years, I decided that I really wanted to go back and finish up my training so that I could get board certified in internal medicine, and I decided that I wanted to go into medical oncology as a specialty. I went back to Stanford, I applied to Stanford for that, and they accepted me back right away, so I went back in '75 and worked there until '77, and I was able to use my research at NIH and count that toward my board certification in internal medicine, in those days, I was able to do that, plus do my oncology training. So, after all that, I was able to become eligible for the boards, what we call our certification process. I took the exams, and became board certified in internal medicine and medical oncology. But my true desire was to get a job in a university, primarily where I could combine research with the practice of medicine. Now, it was in that second return to Stanford that a number of things that were going on around me had a significant impact on me. So, if you want, the birth of the biotech industry really still took place in the Bay Area, where things were really happening. That's where Howard and I were. First of all, I met Howard Birndorf, who was working at Stanford with one of the oncology professors, and I was in training. I was what you call a fellow, a post- doctoral fellow. So, we hooked up together, and did some things together, Howard and I, but…there are some important things that happened, and I'll go through that very carefully, because if we're going to get the record straight here, it's very important to know exactly what happened. First of all, you have to understand the environment that we were in. Genentech had already been started as I recall, in '76. So, I was there from 1975 to 1977.

JONES: And you were cognizant of that?

ROYSTON: I was cognizant of that, because I was cognizant of Cohen and Boyer and recombinant DNA and Cohen was right there, I went to his lab to talk to him. So, I was cognizant of that, and another thing I was cognizant of was Kleiner-Perkins funding Genentech somehow. I think it was through my association with John

Daniels. John Daniels was a faculty member in oncology at Stanford, who I related to a lot as a fellow, and John Daniels was the founder of Collagen Corporation, another biotech company funded by Kleiner-Perkins, also. So I knew of that. So, already the idea that there was a group of people that started companies with professors was already highly visible to me, through Genentech and Collagen both -- Collagen was closer to home. OK, so that was there in my mind. The other thing that happened was, when I got there, a new faculty member arrived when I arrived as a post-doctoral fellow, that was Rn Levy. Ron Levy came as a new assistant professor of medicine. He's now the director of oncology at Stanford, the Division Director. And I asked Ron, 'Well, what are you going to work on?' And he said he wanted to work on this method for making antibodies by essentially monoclonal antibodies, but by a technique called the spleen fragment culture system. What you do is chop up the spleen into small, little fragments and

JONES: This is Milstein's?

ROYSTON: It's not Milstein's. No, in fact, the spleen fragment culture system had nothing to do with Milstein yet, that would come just a year later. It's something that Norm Klinman developed, who used to be at the University of Pennsylvania. He's now here at Scripps, so he's in San Diego, and nobody really recognizes this anymore, and it's really unfortunate for Norm, but Norm Klinman was trying to work on making monoclonal antibodies, but he hadn't discovered the trick that Milstein and Kohler discovered which is making hybridomas, which is to fuse cells together so they could be immortal. What he was doing was culturing spleen fragments, little, small fragments in each little well, getting the fragments small enough so that only one antibody would come out of each fragment. But those fragments wouldn't be immortal, so you could analyze the antibodies, but you couldn't make unlimited amounts. What was missing was the immortalization step, so I was playing around with that idea, too, looking to see if it was possible to identify an antibody that reacted against cancer cells. My interest at that time had evolved from virology to immunology, and that happened at NIH when I was studying mononucleosis. I was interested in the virus that caused it, but then I became fascinated with how the body reacted against the virus, and that's immunology -- how the body reacts. So, I was becoming much more interested in immunology and the immunology of cancer. Trying to understand how the body recognizes cancer cells, and how can we get the body to make an immune reaction

to cancer cells, and that's what we do here today, so thirty years later, we're still doing the same thing. So, I'm working on this system, and then the Kohler-Milstein paper comes out in Nature in 1975, in the fall as I recall. We read it, and it looked really interesting, you know, the idea that you could fuse these cells and make hybridomas, and then those cell lines would grow and be immortal and continually make antibody. It obviously was the answer. I can remember saying, 'Well, that does away with our spleen fragment system.' But I had the idea that we would fuse the spleen fragment with the cell line to immortalize that, but what you could is just fuse whole spleen cells with the myeloma cell line, get a hybridoma, and then you could just clone out that. So, I was very intrigued by that, and so was Dr. Levy, because he turned his lab into trying to confirm those results. And the way we were able to do it was that Len Herzenberg, who was a professor of medical genetics at Stanford was on sabbatical at Milstein's lab that year. He's still there, and you can talk with him, because in order to start this industry, I needed that cell line, so you have to trace the origins of the cell line. First, we have to stop and make sure that we both understand hybridoma technology. The hybridoma is a cell that results from fusing one cell to another, but that hybridoma cell is a cell that makes the monoclonal antibody. So, you just grow the cells up and they secrete antibodies into the supernate. To make the hybridoma cell, we fuse spleen cells with a cancer cell line called the myeloma cell line. The spleen cells from an immune animal that you've been immunizing, has inside of it, the spleen cells, the antibody producing cells. The myeloma cell line is a cancer cell line that's derived from an antibody cell line but it has the properties of being immortal, it's cancerous. You put them together and you have a cancerous cell line that makes antibodies. It makes the antibodies of the parent, and has the property of both parents, the antibody that the spleen cells were making, and the immortality. Now you have a hybridoma cell line that you can grow up, you can freeze it down in liquid nitrogen, and continually make the same antibody, that was the revolution. So Len Hertzenberg brought back from England the myeloma cell line, the immortalizing cell line, to Stanford. Then Ron Levy asked for it, and he gave it to Ron, and since the labs are pretty much open, and I was doing some work with Ron Levy, some experiments. I asked Ron, as a new faculty member, I said, 'I'd like to do some experiments in the lab.' And he says, 'Yeah, come right in, whenever you have some time, come in and do the experiments.'

JONES: Do you go in and watch them do it?

ROYSTON: Yeah, that was part of it, and part of it was just doing it ourselves, and Howard was…I think I had bumped into Howard there, and I had said, 'Howard, you know, we ought to try to figure out how to do this, to make antibodies against cancer cells, because someday we might be able to treat cancer with antibodies.' And finally, today, thirty years later, that was in '75, now it's '97, so twenty-two years later, IDEC, which I've been involved in also, with Ron Levy, has now just applied to the FDA for the approval of the first therapeutic antibody for cancer. So, that's twenty-two years later.

JONES: When do you expect this approval?

ROYSTON: It's going to take six months or so to go through the review process. So, we'll be lucky to get it this year, but later this year, early next year. So, we worked with it in the lab, in Ron Levy's lab, and when it came time to move to San Diego, I basically just took the cells with me. Oh, I left out a very important step -- there were no such things as material transfer agreements in those days. And there was no material transfer agreement coming from England to Stanford. Keep in mind, they didn't even apply for the patent, right? That was one major mistake. What happened is -- I forgot to mention a very important thing -- now you just don't move cell lines around. But when I left NIH, and moved to Stanford to do my oncology training, I had spent three years at NIH, and I had accumulated lots of cell lines that I wanted to use in my research. So I took a liquid nitrogen container and shipped it to Stanford. What I did was to get the government to agree that this was discarded property, or something like that. I forget what the jargon, what the word is to deactivate something, but it wasn't just taken, they knew about it. It was just no longer needed by the government. But I had all my cells in there in liquid nitrogen. I shipped it to Stanford, and I asked Ron Levy, I said, 'Here's my liquid nitrogen tank.' I don't know if you've ever seen one of these things. I can show you one downstairs if you're interested. Because you've got to have the cells, and the cells are shipped at liquid nitrogen at minus 180 degrees centigrade, where they're in suspended animation. They can live in there forever. So I shipped this to Stanford, and I said to Ron Levy, 'Look, you're working in immunology and cancer, and that's what I want to do, and look, I've got all these cells. Someday, I'm going to need them. I need to store it here.' 'And you can use the cells,' I said, 'I've got cells in here that I'm sure you can use in your research.' So, I went over all the cells I had, these are just different cell lines that are well known in the literature, and he recognized them, and

said, 'Oh Yeah, absolutely, I could use these cells in my experiments.' So, I said, 'Well, fine. We'll have a deal. I'll store it here. You'll continue to put liquid nitrogen in the tank as needed, just like the rest of your tanks, while I'm finishing up my training here for two years, and you can use the cells.' Well, at the same time, you know, cells are freely moving around the laboratory. If I wanted to store new cells, I just put them in the liquid nitrogen tank. I can't actually remember when we get right down to the myeloma cells that eventually came down to San Diego and eventually went over to Hybritech, I can't actually remember if I brought those cells down in the liquid nitrogen tank, or whether I asked Ron Levy to ship me a sample of the cells. I think I actually asked him to ship the cells, you know, to my research program. But let me get to that later. So, I became very interested in this whole idea of monoclonal antibodies and as I was finishing my training and recognizing that there was no open positions at Stanford -- Ron Levy had the last position, there were no new positions. I needed to look for a permanent position for myself, now that I had finished all my training, and I applied to a number of universities, and I was most intrigued about the San Diego opportunity. I was accepted here as an assistant professor at UCSD, where they were just starting a new cancer center program, a new cancer program. So, I accepted the job here, moved to San Diego in 1977, brought my liquid nitrogen tank with me. I started writing grants about six months before coming down here, and got some funded, plus I had start-up money from the department here. I was going to be an independent researcher. I had a track record by now. And I offered Howard the job. I said, 'Howard, how would you like to come down to San Diego and be my technician?'

JONES: Why did you pick Howard?

ROYSTON: Well, he had learned the techniques with the monoclonal antibodies. He was very interested in working in this area. And I thought he would help jump-start my program by not having to look for somebody new, especially in a new area, where, probably, no one in San Diego had ever worked with monoclonal antibodies. Which was true. I was the first person to do that. So, in other words, I would be able to bring somebody who had some experience in this area. Because he had gained that on his own. Actually, he had done some experiments, on his own, at night, in Ron Levy's lab, because in the daytime, he was working for Frank Stockdale. I can't remember now where exactly he did the experiments, whether in Frank's or Ron's lab, but we would do some experiments together. So, I offered him the job, and he

accepted, and he came down, and when my moving truck came, I moved him, too. I remember, and he probably told you, when we came down for interviews -- I brought him down for interviews -- we had to sleep on the floor at one of his friend's house. I brought him so he could see San Diego also, he didn't know San Diego. I said 'just come down with me,' and he said, 'I have a friend in San Diego,' and I remember staying over at his friend's house while we were interviewing for the job.

JONES: And you guys were friends at this time?

ROYSTON: Well, yeah, we were friends, we got along pretty well together. But it was more of a -- I always saw him as sort of a research assistant. Of course, things are different now, because Howard's been so successful in his entrepreneurial endeavors in this business, but my relation goes back to where -- he was a master's degree person, as I recall – he always was able to, and he always wanted to do more than, but, it was clearly, I was more of his superior at that time. I mean it has changed since. So, I accepted the job here. I had been offered jobs at several other places, but I accepted the job at San Diego, and moved here, set up the laboratory, Howard came down, and we started working together. So, I had gotten some grants funded, because it was a brand new hot area, monoclonal antibodies and cancer.

JONES: Had you considered other places besides San Diego? Was it the new cancer thing they were starting that was attractive?

ROYSTON: That was attractive to me, the fact that it was a brand new cancer center. I'm always attracted to start-ups, I guess, start-up opportunities, that's why I'm here now. But the other position I gave some serious consideration was in Atlanta, at Emory University, but I opted for San Diego. That's where it seemed like a whole new program was developing. And I was brought in, really, to direct the clinical immunology program of the cancer center. So I became the director, and once the new cancer center building was up, which was in Hillcrest, it's called the Guildred Cancer Facility, I became the Director of the Clinical Immunology Program. My laboratory was originally based in the Veteran's Hospital in La Jolla. So, immediately upon arriving in 1977 at the beginning of the academic year, in July, we started working on monoclonal antibodies made against cancer cells, with the idea that we would try to make antibodies that would recognize cancer cells and not normal cells. I chose for that work lymphoma cells, cancers of the lymph system.

JONES: And why lymphoma, in particular?

ROYSTON: Because I had cell lines that I brought down. I had a number of cell lines readily available in this area to use as immunogens. The way you make these monoclonal antibodies, you have to immunize the mice against these human cancer cells, and eventually take out the spleens of the mice and do this fusion to make hybridomas. Anyway, it worked out quite well. Howard was the research assistant on the project, and he did a lot of the work. We had another research assistant that we hired. It would be interesting to talk with him because he has a whole different perspective on everything. He felt cut out of this whole biotech revolution. His name was John Majda. Did Howard ever mention his name?

JONES: No, he didn't.

ROYSTON: M-A-J-D-A. He eventually went on to become a doctor years later, a radiologist or something, and I don't know where he is. I think he went to the UCSD Medical School. I'm not sure, but they may be able to trace him. You know who would know? The UCSD patent office because we filed a patent, and were getting royalties on one of the antibodies we made, and he was a co-inventor. So they would know his address. And we had another woman who worked with him…[tape ends] I mentioned John Majda. Eventually what happened with the company was that Howard Birndorf left my lab and went to start Hybritech, but John Majda didn't. John Majda stayed on to work with me. He may have been, given what happened eventually, with Hybritech's success, he may have felt bitter that he was never cut into the whole thing, or didn't even get any stock in Hybritech, or whatever, because he probably felt that he was instrumental in the laboratory being successful and then us getting funded by Kleiner- Perkins. That story has never been told.

JONES: You guys never asked him to come along?

ROYSTON: Well, we can talk about it next time when we talk about the birth of Hybritech; why don't we get to that point and stop. So, what happened is, we were making anitbodies against these lymphoma cells, and it was very easy for us to do it, and within six months, by early 1978, we were able to make these antibodies, and they recognized these [cancer] cells, but they didn't recognize these other [normal] cells, and we realized that we could achieve exquisite specificity, and that we could make antibodies that are essentially reactive to these cancer cells. Now, it turned out

that later that they also reacted with certain types of normal cells, but not others, but the point is, we could make specific monoclonal antibodies and once we knew that we could do it, and we were the first in San Diego, I'm sure to do this because, let's face it, Kohler and Milstein just published in '75, and it's already just '77, now Ron Levy was probably doing it up at Stanford, and there were some people doing it on the East Coast at the Wistar Institute, Albert Einstein Hospital in Seattle -- I could maybe count on one hand the number of places that were doing it, but it was brand new technology. But we were the ones that did it in San Diego, and I can remember saying, 'OK, I can see now that we can make antibodies, and we can probably make antibodies that react with cancer cells and not normal cells, or more preferentially with cancer cells -- how am I ever going to be able to treat patients?' And that's where the idea of the company came -- how am I going to be able to manufacture these antibodies? We couldn't do that in the university. We needed big vats and fermenters, and whatever it was that we needed -- lots of mice, there's a technique for making antibodies by injecting them into peritoneal cavity of the mice, and getting fluid. But I realized that we were going to be encumbered by not being able to have manufacturing, and at no point was I thinking that I was going to make a lot of money, or I was going to, you know, build some major industry, I just wanted to manufacture some antibodies. Howard may have thought different thoughts that you'll have to get from Howard as to whether he saw the opportunity to start a business. I mean, I sort of saw an opportunity to start a business. I know that every time I talked to people about a business opportunity, who were in the pharmaceutical industry, they would say, 'Well, we have all these farms with goats and sheep, and what are we going to do with them?' Because we would do away with all that; it was a major paradigm shift. You don't need goats and sheep and horses to make antibodies. What you need is some incubators and some flasks, and maybe some bottles, or maybe a fermenter device, to grow cells. And I realized that is was a major paradigm shift in thinking, and so, it was there that Howard would say, 'Well, let's just start our own business.' I can't say that he said that, because I was familiar with Collagen and Genentech, and maybe I said, 'Maybe we should start our business.' And Howard said, 'Well, I've got friends in Chicago in the options market. Why don't we go talk to them?' And, in my typical compulsive way, I went to the library and got a book called 'How to Start Your Own Business,' and started some of their things. But, anyway, what really happened, what really moved things along, while Howard was in Chicago once, trying to talk to people about the idea, I talked to my wife, and even though I knew John Daniels, I talked to my wife, and told her

about what was going on; I said, 'I really think this is an opportunity to start a new company. That way I could get somebody to manufacture these antibodies for our research.' And she said, 'You know, I used to know this guy, Brook Byers, up at Stanford,' before I got to know her, and 'you know, he's a venture capitalist. What he said is he starts companies. Why don't I give him a call? And she did. And I said to her, 'I'm going to be in San Francisco for a medical meeting, would he have time to meet me?' And with a venture capitalist, since I do venture capital, too, part-time now, you know, you can't just be an unknown person knocking on the door. So she called him and said, 'My husband really has a great idea for a new company, would you be willing to see him?' And I'm sure he was just doing her a favor, and he said, 'Fine. Why doesn't he have lunch with me?' He was a brand new junior partner at Kleiner, Perkins, Caufield & Byers. He was a junior partner, and so I met him for lunch -- in April of 1978. Keep in mind, I just started UCSD in July of '77, pretty fast. Everything was very fast in the whole industry, including when Hybritech got going. Everything moved very, very fast. We were very fortunate. So, in April 1978, I sat down with Brook, and I said the magic words. I remember very distinctly -- because I knew his firm was involved with Genentech -- I just said, 'Look, you guys know how to clone genes, we're talking about the same thing, only we're cloning antibodies. And I sketched on a napkin how to do that, and the point I made with him was, just like you can clone genes, you clone antibodies, because hybridomas lend themselves to cloning. If you clone antibodies, you can make unlimited amounts of these specific antibodies that can be useful for diagnostics and therapeutics. He immediately became very intrigued with the whole thing. You see, it was just the question of using the right words. Because their Genentech experience primed them for another opportunity in immunology. And he said, 'Well, Ivor, go back home, write down some of these ideas on a piece of paper -- it doesn't have to be very long -- and just send it to me. And maybe you can write down what your competition is, or, you know, what's out there.' Well, there was nothing out there. Actually, we found something out there. We found a little, little company called Celltech, they got a small grant from the government, this was in England, that was going to make some monoclonal antibodies, and it had just won an award for best new idea, but it never became successful. I mean, it does exist today, but.... So, we wrote a five page business plan, which became the subject matter of a case study at the Stanford Business School. For many years, I used to go up there to lecture, once a year. That's what was handed out to all the students before I arrived, about how to start a business, and they critiqued it [laughs]. They had all kinds of interesting questions.

It was the only time I've ever lectured where I got a standing ovation. I never get a standing ovation in medical school, but in business school, I get a standing ovation. It was a five-page document. You know, I have a large file at home, you know, memorabilia stuff, that goes back to...I have scrapbooks full of Hybritech memorabilia. Goes back to 1978. Anyway, I sent up that document, and Brook Byers hired a consultant, I was lucky that he hired a liberal-minded consultant, because there were very few people who had been exposed to monoclonal antibodies. They knew nothing about it; it was brand new technology. But he grasped the concept and I know the consultant was favorable, but we got a call back months later, probably at the end of the summer, September, maybe -- that the partners wanted to come down to visit the lab. All four partners -- Kleiner, Perkins, Caufield & Byers -- last time I've ever seen them do something together, because they all eventually split up to do their own thing. But all four partners took a plane down here from San Francisco, stayed at the La Valencia Hotel, came out to the lab where Howard and I, and John Majda, put on a show. We had hybridomas under the microscope so they could look at them. You could see them under the microscope.

JONES: Howard told me that your lab space was very small.

ROYSTON: Very small space. Then we showed them a print-out from our gamma counter with the radio-immunoassays that, you know, the numbers, so you could see the binding of the antibody to the cancer cells. You could see where it was positive, where you had these large numbers, and where it was negative, low numbers, so you could see that there was activity. We basically just spent the entire day walking through the entire process and showed them how we made monoclonal antibodies in the laboratory. And what happened was that led to, basically, that same evening, Tom Perkins, who was the senior partner at that time, even though Eugene Kleiner was there, too. He was much older. But Tom Perkins really is an instinctive type of guy. You don't need a lot of elaboration or anything. He's a shoot from the hip type of guy. He said, 'What is it going to take, Ivor, to make monoclonal antibodies outside of your laboratory, outside the university, in another lab outside?' And, Howard and I had already worked on sort of a budget, and we said, 'Well, we need a couple hundred thousand dollars to do this.' And he said, 'I'll give you three.' Those were his words at the airport. 'We'll give you three hundred thousand dollars -- he was the spokesman for the group, Tom Perkins -- for principle, we'll give you three hundred thousand dollars, now show us you can make some antibodies outside of

the lab. What's the most common antibody used today in medicine?' It was hepatitis antibody because every unit of blood is screened for hepatitis antibody using an antibody test kit, so I said, 'Hepatitis, we'll make hepatitis antibodies.' And so, he said, 'We'll give you three hundred thousand dollars' -- I had asked for two -- 'and we'll own sixty percent of the company and you guys -- you, Howard, and all the future employees will own forty percent [laughs]. That's the part I was criticized on by the Stanford Business students. Well, we had no money, we were unknown. We were unknown scientists, no track record. Just a couple of guys with an idea.

JONES: So, not such a bad split then?

ROYSTON: Well, no. I mean, in retrospect, no, since they added so much value into -- you know Brook Byers would come down and be the acting President, and really put the management team together. They paid for that, so there all these hidden values that are not on the balance sheet. So, it wasn't so bad. I mean, today, would I do it for that? No, I mean, I would demand...I'm not an unknown with no track record. But, Yeah, in those days, everybody did well including Kleiner-Perkins. Kleiner-Perkins did very well, and I was very fortunate, and so was Howard. I had a bigger stake in it than Howard because of my seniority. But Howard has gone on...you know, these are all stepping stones. So, the company gave birth at that point to the idea ...I was excited because it was something brand new, and there was the possibility that this could help me with my research developing new ways to treat cancer. There was actually going to be an organization in San Diego that could actually work just on this, and the plan was Howard would quit, go on into the company to help set it up, which he did, you know, hire scientists, get some space, which we did at the La Jolla Cancer Research Center, which is now the Burnham Institute, right around the corner here. I would become, basically, the acting scientific director, do it on my spare time. You know, I was an assistant member of the faculty, wanted to be tenured someday, now going out to do something that no other medical professor had ever done before, here in San Diego. At Stanford, they did -- Boyer, Cohen, John Daniels, so I knew it was doable. It just had not been done here in San Diego. So, that was the birth of Hybritech, and the money was received in October of 1978. So, I went to see Brook Byers in April of 1978, it was funded in October of 1978, that was the day Hybritech started as the first biotech company in San Diego.

JONES: What did the university say?

ROYSTON: I got all the check-offs and all that. We had lawyers review all that stuff, and we can talk about that, because there was the backlash, I mean, as it became more and more known within the university that I was doing this, there were people that were very disgruntled or people who were unhappy, you know, 'how can I possibly do both?' We can get into that next time, if you like.

INTERVIEWEE: **Ivor Royston**

INTERVIEWER: **Mark Jones, PhD**

INTERVIEW: **Part 2 of 3**

DATE: **June 23, 1997**

LOCATION: **San Diego, California**

ROYSTON: It seems to me that in discovery there's always more people involved, or in any activity, than some people get credit for. I'm going through that now with somebody else, so, there's always somebody who feels that they're not getting appropriate credit.

JONES: When you came down here, John Mendelsohn was the person who brought you down here?

ROYSTON: John Mendelsohn hired me, yes.

JONES: Did he bring you specifically to work on monoclonals?

ROYSTON: No.

JONES: Did he know about monoclonals at the time?

ROYSTON: Yes. When I applied for the job, I told him that that's what I wanted to work on, and he liked that idea.

JONES: But it wasn't like they were looking for a monoclonal person?

ROYSTON: No.

JONES: Well, when we left off, you had just received the money from Kleiner-Perkins, and Howard had left to put the company together.

ROYSTON: Yeah, Howard decided that he would leave the job at the university, the VA, and go work for the company full-time. And by now, we'd already gotten some money, we've covered that right?

JONES: Right.

ROYSTON: We'd gotten funded, and he was able to leave and basically set up shop. We did that over at La Jolla Cancer Research Foundation, right up the street here. Howard went in there and asked them if they had any lab space to rent, and they did. And that's where we set up an office and a lab. It's that simple. Of course, many years later, a lawsuit erupted between Hybritech and La Jolla Cancer Research Foundation. I don't know if you know about that?

JONES: No.

ROYSTON: As to who invented the two-site radioimmunoassay, what we called the TANDEM, and they claimed, La Jolla Cancer claimed that they had put out the first, Hybritech said that they had developed it. The only people in the world who said they had developed it were right next to each other, so the implication was that one stole it from the other.

JONES: Was this because Gary David had been associated with La Jolla Cancer?

ROYSTON: No, but the labs were right next to each other. The person to talk to there is Eva Engval, the companion of the Director over there, is the person who probably knows the most about that. I don't know if you want to get into that.

JONES: Well, perhaps.

ROYSTON: Well, La Jolla Cancer was involved, and that was a lawsuit that had been ongoing for some time.

JONES: Was it resolved?

ROYSTON: I don't know. I don't know what the resolution of that was. I don't know if it's still pending or not. Anyway, yeah, we –y6tset up shop over there, and one of the first things Howard did was to hire Gary David, because we wanted a radioimuunoassay expert, somebody who knew how to work with antibodies

JONES: Did you know Gary David before, or know of him?

ROYSTON: No. I'm not sure how Howard found him. You'll have to ask Howard about that. I'm don't remember if Gary was already working over there, if he had left Scripps. He was trying to set up his own little company.

JONES: Yeah, I talked to Gary. He was exchanging lab space at La Jolla Cancer for doing some consulting or something.

ROYSTON: Exactly. So, we met him over there, and said, basically, 'Why don't you come work for us,' that kind of thing. He was very good. He was very instrumental to developing the products. And my recollection is that we did transfer the cells from UCSD to Hybritech, and in those days, there were no material transfer agreements that we had to sign. Today, you would have an agreement of some kind. And usually those agreements say you won't commercialize it without approval of the institution, but those things were not in place. The cells were transferred from Stanford to UCSD without a material transfer agreement, they came from England to Stanford without a material transfer agreement, so they came from UCSD to Hybritech without a material transfer agreement. So, in your analysis, in your study, if I were focusing on it, I would talk about how things were done then as opposed to how things are done today. Now there are procedures and policies in place, in most institutions, that require you to say, if you're going to transfer biological material or some piece of property from one institution to another, it is usually done under, you know, with a material transfer agreement that both organizations sign, that stipulates what the rights are.

JONES: Somebody actually wrote a book, a chapter in it is about the Hertzenbergs distributing cell lines.

ROYSTON: What book was that in?

JONES: It was called Exquisite Specificity.

ROYSTON: I've heard of that.

JONES: Yeah, it was done by a couple of guys up in Montreal, at McGill, who do social studies of medicine.

ROYSTON: Yeah, so anyway, with that completed, then the cells were then, I think we probably hired some technicians, the cells were started to be grown, and experiments were done, and I would come over, usually in the afternoon, late afternoons, to sort of look at the cell cultures and the lines, because they didn't have a biologist on board yet, and made sure everything was going well, so I did sort of my consulting. I remember sort of getting calls, you know, 'Can you come over and look at these cells?', and I'd say, 'Yeah, they look good,' or whatever, so I was sort of a doctor to the cells. I know that we went out and hired, we started recruiting people, we hired Joanne Martinis, who was a really good cell biologist from Philadelphia, from Wistar Institute, and she started taking over more of those functions.

JONES: And you knew about her? You were familiar with what they were doing at Wistar, and you knew her?

ROYSTON: Right, and I also interviewed her when she came out here. I interviewed most of the people in those early days. Anybody who got a job with Hybritech early on, I interviewed.

JONES: How did you convince her to come to Hybritech, you know, this little start-up?

ROYSTON: Well, that's a good point. I think she appreciated the future of monoclonal antibodies. She was an expert at cell hybridization. They probably had started doing that at the Wistar Institute, because the people at Wistar started Centocor. Maybe she was not being involved with that, no, I think she saw that we knew what we were talking about, and realized the potential, the future, was there, and I'm sure she's in San Diego someplace, you could talk with her.

JONES: Actually, she's in Seattle now.

ROYSTON: Seattle?

JONES: Teaching school. She lives on one of those islands, the San Juan Islands.

ROYSTON: She teaches school there? It would be interesting in your study to show where everybody went.

JONES: Well, that's what I'm going to do, yeah.

ROYSTON: Yeah, what happened to each of their lives. We could do a movie on it someday. Gary, I know is consulting today.

JONES: He's getting ready to start…

ROYSTON: Another company?

JONES: Yeah.

ROYSTON: You should tell him to call me.

JONES: OK.

ROYSTON: Just to see if I can help him. So, you know, things went on. I think the next big, my recollection is that the next big thing we had to do was to get a CEO in place, because Brook Byers would come down every week, spend a day or two, make sure everything was going all right, as the acting President. Then I remember him calling me, saying that he heard that there was this guy in Orange County who wanted to start a monoclonal antibody company by the name of Ted Greene. I'd say this was about four or five months after we had started. And that they were asked to look at, some guy from Baxter. Well, it was Ted, and Brook asked me, and I didn't know remember if Howard went, and possibly Howard did go, to go up there with him and meet with Ted Greene, to see if what he was planning to do, and that possibly we could attract him into the company so they wouldn't start a competitive company, since we needed a CEO, and he seemed to be the kind of business guy that one would be looking for. So, that's exactly what we did, and he told us to meet him at his apartment on Balboa Island in Newport Beach, and that's where we met him, and we talked, and he seemed interested, and he said that he had partners that he had to deal with, and he'd have to talk with them. But, one thing led to another and he decided to accept the offer being CEO of this company. I think he was attracted to the fact that we had everything up and running. He didn't have the cultures going, he didn't have the scientists, he just had the idea. But we had everything up and running and we had the venture capitalists, Kleiner-Perkins had already invested in us, and think he saw the opportunity to come in and be the President of this company, the CEO of the company, and fulfill his aspirations, and that's what happened. He accepted and he came down.

JONES: And you liked him?

ROYSTON: Yeah, he was very personable. For a marketing guy, he was knowledgeable, he was intelligent. As I got to know him, though, you know, he's somewhat dogmatic about things, but he's a pretty smart guy, and he was a good speaker, an articulate spokesman for the technology. So, he'd make a good outside person, to talk to outsiders. As it turned out, within the company, there were some issues as to whether, as David Hale grew up within the company, who would be the better day-to-day operator of the company, as David felt that he could do a better job, so eventually, Ted was bumped up to Chairman, well, Chairman/CEO, and David became President and COO, I guess. But David was brought in as head of marketing, David Hale. Anyway, Ted Greene, once he was on board, he said to me, you know, I was still pretty active with them, and I was still the acting R&D director, because there was no head of research, so I still chaired a weekly meeting, I'd come over there, get all the others, Gary David, Joanne Martinis, and chaired a kind of weekly scientific session.

JONES: Gary David told me that you kept the minutes for these meetings.

ROYSTON: I did.

JONES: Do you think that they still have them over at Hybritech?

ROYSTON: They were subpoenaed in a lawsuit, various lawsuits, and so I don't know, personally, what happened to them. They would be at the company. And, oh yeah, Ted used to be, you know, we started the company in 1978, in October, so now we're into January, February '79, Ted was on board, and over the next several months, he said, 'You know, we really need to bring on a real experienced research and development director that can, that knows how to make products, and things like that, and the person that he wanted to hire was somebody he knew from his past, Tom Adams. Of course, Tom has just recently resigned as CEO of Genta. So, that was really tough. Tom, at that time, had a position at Technicon, in New York, and he was very slow to respond. He came out to visit, but wasn't sure. It took quite a number of sessions with him, meeting with him, and I participated in some of them, and in calling him, then after enough pestering he decided to take the position. He came out, and his expertise was in developing diagnostic kits, he was a chemist by training, and the use of antibodies for developing these kits. The one nice thing about Hybritech, when I conceived of Hybritech as a company that would make antibodies, and help us with our research, you know, try to treat cancer

patients, and we wrote the business plan, and Kleiner Perkins said, well, you know, we'd sell antibodies in a bottle, but what they quickly conceptualized was that the real power of the antibodies was to use them as ingredients in special diagnostic kits. The value in the actual cost of the antibodies was just pennies, in terms of making the kit itself, with all the plastic and the glass and the bottles, because such minute amounts of antibody were needed, you know microgram amounts of antibodies, so you could make very large amounts of test kits with a small amount of antibody. So, they conceived of using these antibodies to build better diagnostic tests, and we embarked on a variety of these types of tests, pregnancy tests, CEA tests, and of course, prostate specific antigen, the PSA test that put Hybritech on the map. What was really interesting, I don't know if I mentioned this, is that when we received the money from Kleiner-Perkins, and they wanted to use this money as what they call proof of principle, 'Here's three hundred thousand dollars, show us that you can make antibodies in the company, outside the university. And we said, 'Fine. We've just got to decide what antibody to make.' And we said, 'Well, let's make hepatitis antibodies because the number on antibody used at that time was hepatitis. Every bag, every unit of blood, every blood transfusion required testing for hepatitis, and that was an antibody based test. You mixed the blood with the antibody for hepatitis to see if there was a reaction. If it was a positive reaction, that meant that you had hepatitis in the blood. So, you'd have to screen, there's a lot of blood to screen. This, of course, was before HIV, and now, of course, we have do that with HIV, as well, and other hepatitis viruses, but what was really interesting and it shows you the credit of someone like Ted Greene, I don't know if I mentioned this before, we succeeded in making the hepatitis antibodies in record time, and Gary David, I give Gary David a lot of credit for that, and the rest of the staff, but Gary was able to characterize the antibodies very quickly once they were produced, and we had antibodies to the various subtypes of hepatitis, the only thing, what was very interesting, is once Ted Greene was on board, it was just natural to assume, 'OK, we're going to make hepatitis test kits,' and sell them, because that was the number one test. But Ted Greene said, 'Nah, I don't like that idea. The worst mistake you could make in this business would be to go head to head with Abbott, which has the market share of hepatitis testing. Abbott will find some way of getting around you, getting antibodies of their own, and they'll just kill you. We shouldn't do that. We should work on another test that Abbott's not focused on.' And so, he, as the President of Hybritech, he made the executive decision, supported by the Board, I think, that we would not use those antibodies to develop a product, a test. We'd sell

them, if anyone wanted to buy them in a bottle, but we wouldn't use them. And, in retrospect, when I think about that, that was the right decision, because Centocor eventually made hepatitis antibodies and they licensed them to Warner-Lambert, and Warner-Lambert tried to market them against Abbott, and they got killed. Abbott has their own antibodies now. One couldn't get a patent, I guess, on the antibodies themselves, but what Hybritech did develop, of course, was that two-site TANDEM assay, which, of course, Abbott has been fighting, which there have been lawsuits about, and also J&J, but making products such as CEA, PSA, pregnancy tests, that was much a more lucrative area, and not battling with Abbott on hepatitis. So, in retrospect, I think that decision was the correct decision, and it shows you the importance of bringing in sound business people who knew how to make the right business decisions, and not let the scientists try to run the company. I've seen too many companies go bad because the scientists had too much influence. Scientists really are not necessarily the best business people and what makes a successful company is the marriage of the science with the business world, scientists and business people working together.

JONES: In the biotech field, this was a problem early on, but it's getting to be less so?

ROYSTON: Yeah, it's getting to be more readily understood and appreciated. So, we began, the company began making those other tests and the philosophy of the company was that, long-term, the company would make therapeutic antibodies to treat disease, but short- term, we would develop diagnostic products that one could sell quickly. There was less regulatory interference, or fewer regulatory barriers to approval, and to start generating revenues. So, it still took quite a while to get these products approved, but not as, they never fulfilled their mandate of getting a therapeutic antibody into the market. It was already bought by Lilly, and then Lilly got out of the business, and it was a big mess. But, as I've said to everybody, though, Hybritech did, by making the PSA test, contributed enormously to medicine in the United States. It's because of that test that prostate cancer is now picked up so quickly and easily in younger men. In the old days, prostate cancer wasn't discovered until you were in your seventies, you know, maybe late-sixties, now you're picking up prostate cancer much earlier. The PSA test has really revolutionized the detection of prostate cancer, and that has come about because of these diagnostic kits that

Hybritech developed. Abbott makes their own now, but that was a major contribution that Hybritech made, I think, to society, so I was very happy about that.

JONES: Well, after a number of these kits were on the market and started generating revenues, were there any discussions at the Board level about, you know, maybe we should just stick with this, and develop this, this is a good thing and there's still plenty of room to go further, rather than get into imaging and therapeutics, which could be a big drain on the company?

ROYSTON: No, we never had a discussion that I can recall where we said that we were not going to do imaging or therapy because the feeling was that the value that the market put on Hybritech, it valued it as a pharmaceutical company. If we had told the market that we were only a diagnostics company, the market value would have come way down, the stock price would have fallen significantly, this is once it was public. I don't recall that kind of discussion taking place. I always recall that there was a commitment to imaging and therapy, first imaging, that's right, and I don't recall that ever changing. In fact, you know, Eli Lilly built a large plant, a manufacturing plant for antibodies in anticipation that there would be antibodies injected into patients for imaging colon cancer, for example.

JONES: Did they do that in Indianapolis?

ROYSTON: No, here in San Diego. And they never used it. So, that was Eli Lilly, but it was at the end of, it was in 1986 when the merger with Eli Lilly was taking place, so this was just eight years after founding Hybritech, and eleven years ago now, that's interesting when I think about it. It does seem like a long time ago, actually. Some things seem like they go so fast, but the Eli Lilly merger seems like a long time ago. Anyway, I was very interested in treating lymphoma, cancer of the lymph system, with antibodies, and Hybritech was going through the Eli Lilly acquisition and they didn't want to get involved with lymphoma. First of all, it was a small market, and they felt that it was not something that Lilly wanted to do. So, that led me, also, to get involved in starting IDEC. Now, I'm very happy, because IDEC is going to the FDA next month, and so, if you think about, I started this company with Howard in 1978, with the idea that we would treat cancer patients with antibodies, and it never got fulfilled with Hybritech, and then in 1986, when I realized that it was not going to happen with Hybritech, I was able to convince Kleiner-Perkins and others to start IDEC, with the express purpose of using antibodies clinically, therapeutically, and

targeting lymphomas, where I thought it would be every effective. And now, 1997, IDEC is going to the FDA, next month, July 25th is the meeting, an advisory committee meeting to request approval to market the drug. Now, I'm expecting the advisory committee to be very positive about it, because the data looks very good, and the FDA, later this year, will approve the marketing of the drug, so it will show you that, from the time that we conceived of using antibodies to treat cancer in 1978, till the time that it will be approved for the treatment of cancer, will be 1997, nineteen years, twenty years.

JONES: Is this the product here? This is the IPO prospectus, it was in Phase III then.

ROYSTON: No, that product was dropped because it was a customized antibody, no, it was a pseudo- customized antibody, and it was dropped in favor of this one, no, not this one, it's not even on there. It hadn't even been introduced yet. Another antibody came along that they called anti-CD20, C2BA, yeah, it evolved from this line, and it wasn't listed in the IPO then. Yeah, that's what going in. When was this IPO, 1991? So, that means they were able to make this antibody and do the clinical trials from 1992 to 1997, probably.

JONES: Well, let me back up and ask you a couple of questions. When Ted Greene was thinking about starting his company, Cytex, he says that he went to see somebody at Irvine, a guy named Jim Watson to talk about monoclonals. Did you know him?

ROYSTON: I know who Jim Watson is, but I didn't interact with him. Jim was not one of the early guys. He worked a lot with growth factors and, I mean I've heard of him. He was a well-known scientist at UC-Irvine.

JONES: But he wasn't sort of in the monoclonal community?

ROYSTON: Not that I can recall.

JONES: In the early days, did Tom Perkins dominate the Board meetings? Is that your recollection?

ROYSTON: Tom was the dominant figure, yeah.

JONES: Even though officially the Chair was…

ROYSTON: Brook Byers.

JONES: Did you learn a lot attending those Board meetings?

ROYSTON: That was my first exposure to capital and business at that level, yeah. I learned a lot. And right now, in addition to directing the Cancer Center, I spend part of my time being a partner in a venture capital firm called Forward Ventures, and Tom Perkins, I think, was a very intuitive person. It's not like he had to do extensive due diligence, you know. Once he got comfortable with the technology, intuitively, and it made sense, and he got comfortable with the people, he was willing, basically, to bet on that, to bet on you. I don't know if I told you, but when they all came down to visit our labs and we went to the airport, I remember it was Tom Perkins who said, 'I'll give you a couple hundred thousand.' It wasn't like, you know, today you have a partner's meeting, and you discuss every company, but to just go down to the airport, and for a guy to say, 'OK, let's do it.' You know, he clearly must have been, he clearly was the dominant person. I admire that kind of thing. I think more and more people should, you know, instead of doing extensive due diligence, should just trust their instincts, their gut, you know, 'Let's do it,' because, in the end, you know, you can weigh all the risks, and there are always risks involved, and, in the end, it comes down to a very intuitive feeling about whether you want to invest or not. You're investing other people's money, but they've had a very good track record. And so, I admire Tom Perkins, and his intuitiveness.

JONES: Well, this is getting way ahead of the story, but now, at Forward Ventures, do you try to invest intuitively? I mean, how do you evaluate people and technologies?

ROYSTON: I try to think of Tom Perkins when we do things, because in the end, I can go nuts trying to decided, you know, we always see things so early that there's no way to be sure that something's going to work or not, so it always does come down to an intuitive feeling about whether you think it's going to work, if you're a technology based company, that the technology will actually, and you have to have a feel, then, for the technology. So, yeah, I tend to try to rely more on those feelings than on extensive due diligence, every fine point.

JONES: And which would you say is more important, the people involved or the technology?

ROYSTON: That question is asked a lot. And invariably, you'll get the answer from most people that it's the people. The idea is that if you invest in the right people and the technology doesn't work, then the people will find new technology, from an investment perspective, whereas if you have good technology and the wrong people, the technology can really flounder, and I've seen a number of examples of that. I've heard of a number of others. You can have some excellent technology, but the people can really screw it up. And sometimes, that technology never actually comes out, it never finds a place. So yeah, you would invest in people over technology, the best, but if you're investing in a technology company, there is, of course, a coming together of the right people with the technology, and then you'll have a winner. The hard part for us at Forward Ventures is deciding is the basis of a standalone company, whether it has the breadth and depth required to sustain itself as a standalone company and attract other investors, as opposed to being a small area that should be part of something else. You know, breakthrough technologies don't come along that often. Forward Ventures just invested in something that we're really excited about in Boston that we think is a very exciting new technology, but, you know, monoclonal antibody technology is in the same vintage as, you know, recombinant DNA, genetic engineering, and those things just don't come along every day. So, we were fortunate. There are other monoclonal antibody companies besides our own, of course, though we were fortunate to be part of, one of the first ones. Others were like Genetic Systems in Seattle, Centocor, Monoclonal Antibodies, Inc., which Hybritech went to battle with.

JONES: And you were cognizant of these things going on? Did you know the people involved?

ROYSTON: I didn't know Bob Nowinski personally. I knew him by reputation. I knew the people at Wistar, I knew Hilary Koprowski, Carlo Croce, who's my counterpart. I'm at Sidney Kimmel Cancer Center, Jefferson is where Carlo Croce is now. I knew them. I did not know the guys at Monoclonal Antibodies, Inc., but we were one of the first few companies that got started about the same time. There were only about a dozen people in 1977 who knew how to make monoclonal antibodies, and I was one of them. I already traced that lineage for you, of how, most people don't get into all these details, but it's sort of interesting how Hertzenberg was on sabbatical and brought the ideas to Stanford, and Ron Levy picked it up, and Ron is now the Chief of Oncology, and he was a co- founder at IDEC with me, and I was in

Ron's lab at the time, Ron Levy's lab at Stanford, that's where I met Howard. I got the cells from him. It's interesting. There's a lot of serendipity here, you know, a lot of luck. A lot of being in the right place at the right time. Would I ever be, you know, what would have happened had, would there have been a biotech industry had I not moved to San Diego? Who knows? I mean, I guess there would have been, eventually?

JONES: It might have been very different. It might not be what it is now, to the same extent.

ROYSTON: Look at Irwin Jacobs at Qualcomm, you know, that appears to be a very successful company, I mean the thing that we, with Hybritech, I mean now, we have all these other companies that want to move to San Diego, so that's nice. I don't know what would have happened. It's interesting that a monoclonal company of any stature did not appear in the Bay Area.

JONES: Well, Monoclonal Antibodies, Inc. was there, but I don't know very much about them.

ROYSTON: It was a very small company.

JONES: Well, there were some other things going on around here shortly after Hybritech, you know, Synbiotics, Molecular Biosystems? What was your perception of those companies? Did they make much of an impact?

ROYSTON: They didn't make much of an impact on me at the time. Yeah, I don't know which, I was aware of them. Synbiotics, I was aware of all of them, but I was not involved with them, so....

JONES: Well, they certainly never had the kind of success that Hybritech did.

ROYSTON: It's interesting that Hybritech was sold to Eli Lilly for a whole bunch of different securities, and it actually amounted to about 400 million dollars in stock, convertible bonds, warrants, whatever it is, that's what basically ended up happening. It doesn't seem like a lot of money today when you read about mergers and acquisitions, today in 1997.

JONES: Well, at the time, this was the largest sale price for any San Diego company, and actually the company that topped that is Pyxis, which also has got the Hybritech connection.

ROYSTON: Yes, Pyxis, that's a real interesting story. As I understand it, Tim Wollaeger came up with that idea by talking to a nun. Did he ever tell you that story?

JONES: Yeah, he did. Actually, I've heard two different versions of it.

ROYSTON: A nun that was waiting to…

JONES: Well, Tim's version is that she was a Roman Catholic nun. Ron Taylor tells it a little differently.

ROYSTON: Here's the co-founder of IDEC. Bob Sobol. Come on in, Bob. This Mark Jones, he's writing the history of the biotech industry here, and he'll want to interview you about IDEC. Just so you know, Bob works here, you can catch him here. Mark has interviewed Howard and Ted Greene, Ron Taylor, Tim Wollaeger, Tom Adams, everybody. He's going to do the official, authoritative version. Does Ted still call himself a founder of Hybritech?

JONES: Well.

ROYSTON: When I challenge him on that, he says, 'Well, spiritually, I should be." But it's such a stupid thing, I mean, to say, essentially, if you come in four months after it's founded, then you're there with it to the end, then you're essentially a founder.

JONES: Well, I'm going to tell how it happened, and readers can decide who's a founder and who isn't.

ROYSTON: It's funny because some people come up to me and say, 'Oh, you were involved with Hybritech.' I say, 'Yeah.' And they say, 'Yeah, I met the founder of Hybritech the other day.' And I say, 'Who's that?' They say, 'Well, that was Ted Greene,' and I say, 'Oh, OK.' And then they say to me, 'What did you do at Hybritech?' I don't know how to answer that, you know, do I say, 'I founded it, too, with Ted Greene,' or, you know.

SOBOL: You should say, "I'm the real founder.' Ivor's too modest to say that.

ROYSTON: Anyway, Bob came down to San Diego when I was— OK, Hybritech was started in 1978, 1980 you came down, is that right?

SOBOL: I was here as a medical student before that.

ROYSTON: And when did you come back to do a fellowship with me?

SOBOL: I came back in '80.

ROYSTON: OK, so two years after Hybritech was started, Bob came to work with me in my lab at the university, at the VA, so Hybritech was already started, and Bob was ready to do his oncology fellowship. Actually before, or was it post-medical school?

SOBOL: It was a research fellowship.

ROYSTON: A research fellowship before he went into his internship and residency. He was at Chicago before that, so that's where I met Bob, and Bob and I have had an association ever since, so that Bob went, actually did his research fellowship with me, and I think he worked with monoclonal antibodies, as I recall, and then he went, this is very interesting, because Bob is quite entrepreneurial since his association with me, then he went back to do his internship and residency in internal medicine, and his medical oncology fellowship, all of that, so now he's a board certified medical oncologist like myself, actually did his research fellowship with me, but in 1986, when we started IDEC, you were, had you already finished your residency?

SOBOL: I had finished my internship, but had not done my residency.

ROYSTON: Oh, that all took place after IDEC. So, you did a research fellowship…

SOBOL: Then I was on the research faculty at UCSD, and I left UCSD to go to work at IDEC.

ROYSTON: OK, so we started IDEC, but he left, just like Howard did.

SOBOL: I left UCSD to become a full-time employee of IDEC.

ROYSTON: And we list Bob as a co-founder along with Howard, actually Howard's role in IDEC was pretty minimal, but we gave him, it was sort of like trying to get the old guys back together again.

SOBOL: Howard was instrumental in the beginning. He helped us. He taught me the things…

ROYSTON: I was trying to reproduce Hybritech with IDEC, only I was much busier now, I had more responsibilities, so I needed another Howard, except Howard was already doing his thing, as I recall, Howard was already pretty successful, so here's this young guy, Bob Sobol, wants to be, wants to follow in my footsteps…

SOBOL: And brighter than both Ivor and Howard put together. You can take that part out, that's just…

ROYSTON: And, Bob did not have a permanent faculty appointment, and he had to finish his residency and internship, so those were real negatives in a clinical department, so he decided that he would leave and help start IDEC, and became the first employee of IDEC, and then, just like Hybritech, we would up later interviewing Bill Rastetter for the Presidency of IDEC. And I think you interviewed him, also, didn't you, Bob?

SOBOL: Yeah. We all participated in the hiring.

ROYSTON: Now, the other major event at IDEC was the three of us, that's Howard, Bob, and I, getting the company going, just like we did with Hybritech, and Bob found a little warehouse, set up shop, and it was Richard Smith's old place, called CNS, Center for Neurological Study, in Sorrento Valley, so that's where we set it up, but at the same time, we learned about Ron Levy and Richard Miller's company at Stanford.

SOBOL: There are few things I still have to do, so I have to go. If he says good things about me, they're true, if he says bad things about me—

ROYSTON: Are you still planning to stop by? Shall I call you when we're finished?

SOBOL: Yeah.

ROYSTON: So, yeah, with Bob, we tried to reproduce that system that worked, and then, the only difference here is that Ron Levy and Richard Miller at Stanford were doing their own antibody lymphoma company, and just like we did with Ted Greene, Brook Byers had already invested in us, Kleiner-Perkins had come in, and I got Venrock to invest. I flew to New York, too, to convince Venrock to invest in us, at the request of Brook Byers. And we decided that we should try to see if we couldn't merge with those guys, so there would be just one company, instead of two competing with each other. So, that did happen, but it was a much more complicated merger since they had already incorporated, they had investors. It was a real merger of two entities.

JONES: And you had known about what they were doing?

ROYSTON: I think I knew some of it.

JONES: I've heard that there was a stumbling block in getting IDEC funded because of the proprietary position. Was this because of what these guys were doing?

ROYSTON: No, it had to with the yttrium part. One of the proposals with IDEC was that we would use yttrium labeled antibodies to treat lymphoma. It's in the IDEC product list, here. The yttrium technology had been developed at Hybritech, and since it wasn't going to be used, I wanted to get that transferred out of Hybritech into IDEC. There were other people that had that technology, which I thought was the easiest way to go, and I think you're referring to the fact that it took a while to get Hybritech to agree to make that available, and in return, Hybritech received stock in IDEC.

JONES: Was that critical for getting Kleiner-Perkins to put the money in?

ROYSTON: It was critical, yes, I think it was. And then the technology that Stanford had, that Ron Levy and Richard Miller had had to do with making these customized antibodies, or their technology for making it, but we had our own. I think the stumbling block was primarily the yttrium, but I think it was felt that it would be nice to have Ron Levy's technology in the company as well.

JONES: After Hybritech started, and you were over at the Cancer Center and at the VA working on, doing your research there, you developed the T101 antibody?

ROYSTON: Yeah, that was developed at the university, at the VA. That's where John Majda was involved with the development of that, Gail Yamamoto. We filed patent applications on it. It was one of the first T-cell antibodies that was developed. At the same time, of course, we realized that other T-cell antibodies were developed in places like Dana Farber, and elsewhere, and anyway, we licensed that to Hybritech, through an official licensing procedure.

JONES: And you used this antibody for many years, right? What were the characteristics of this antibody?

ROYSTON: Well, one of the characteristics, it was an antibody to an antigen that's now called CD5, and one of the characteristics of this antibody was that it not only reacted with T-cells, it reacted with a leukemia cell called CLL, chronic lymphocytic leukemia, which is typically a B-cell disease, but, there seems to be an exception. There's a subset of, apparently, B-cells that carry both the CD5 molecule, which is normally found on T-cells. Anyway, it turned out that it was not the best antibody for marking T-cells, because antibodies like CD3, CD4, and CD8 were better antibodies. Ortho made some antibodies and Colter [?] made a set of antibodies. It was Ortho, Coulter, Becton, made, licensed, distributed these antibodies. So T101 was the antibody that we took to the clinic to treat patients with leukemia, T-cell leukemia, a T-cell disease called Sezary syndrome, or cutaneous T-cell lymphoma, and also CLL.

JONES: And Hybritech was using this too?

ROYSTON: Yeah, they didn't really make a business out of it though.

JONES: They never had a therapeutic product.

ROYSTON: Exactly, but we did use it as a research reagent. And people did buy it for research purposes, because I did get royalty checks, so I know they were paying royalties back to the university.

JONES: How would you describe the due diligence that Kleiner-Perkins did when you wanted start IDEC, as opposed to Hybritech? Had the situation changed?

ROYSTON: That's a good question. I think there was more due diligence done at Hybritech because it involved unknown people and an unknown technology. And

then, at IDEC, I don't know, of course, all the due diligence that took place, but it was a little bit easier. It wasn't that easy. It took just as long to get it started, I mean, it was, when you're dealing with known people, you know, trust then is a little easier. That's why Howard, I think, has been able to do what he's done. It's the relationships. People just sort of trust the other individuals. There's a tendency for people who have been successful in one enterprise to repeat that, and venture capitalists like that.

JONES: So, you went to talk to Tony Evnin…

ROYSTON: Yeah, at Venrock.

JONES: How did you present these ideas to him? Was he receptive or was it a tough sale?

ROYSTON: I think it was, I had to, I think, it's hard to remember, exactly. They asked good questions. I had to really explain things to them, and I think the meeting went well and they were receptive to the idea. They had invested in Centocor, so they understood monoclonal antibodies. So when you talk to people who understand monoclonal antibodies, they're receptive. So, yeah, it went well, and their commitment came pretty quickly afterwards.

JONES: And Pitch Johnson had invested in Hybritech. Do you recall when he…

ROYSTON: Did he come into IDEC as well?

JONES: He did, yes.

ROYSTON: That's right, we invited Pitch in, for old time's sake, sort of like a repeat, that's right. Pitch was on the IDEC board, yeah. Was I on or off of the Board at this time?

JONES: You were on, I believe, at the time of the IPO.

ROYSTON: Yeah, but I did go off pretty quickly after that. Anyway, Pitch Johnson, that's right. OK. Pitch Johnson was on the Board of Amgen, too. He was one of the early Board members. That was his big success. So, we had Pitch Johnson, Tony Evnin. I guess I must have told Pitch about it.

JONES: You did go off the Board. Did that sort of sever your ties with IDEC, I mean, you wouldn't be directly involved anymore. Why did you decide to do that? Were you just getting too busy with other things?

ROYSTON: Well, yeah, I think that once the companies go public, well, first of all, Bill Rastetter wanted to have experienced pharmaceutical guys on the Board. He didn't want a big board, so he wanted some rotation. So, it was logical for me to go off. I wasn't interested in being on a board where my contribution wasn't valued. I think that when a company goes, I think that my contributions are better off in the early stages.

JONES: Scientifically, entrepreneurially?

ROYSTON: Well, both, but mainly scientifically, but when it starts getting into real product development and marketing, that's not my forte.

JONES: Yeah, do you lose interest? Do you have less interest?

ROYSTON: Yeah, I have less interest in that.

JONES: Than in discovering?

ROYSTON: Exactly. So I do recycle myself. I've gone off, the same thing happened on the Sequana Board. I went on the Board of Sequana, and then when it went public, I went off that. I went on the board, I think it's happened with another one, too. Combichem, yeah.

JONES: That's a Forward Ventures company?

ROYSTON: Yes.

JONES: Well, Rastetter came from Genetech. Was Kleiner-Perkins the important connection there?

ROYSTON: Right. Yes, they were aware that there was this guy at Genentech that was anxious to do his own thing, and he was in charge of their joint venture operations, putting joint ventures together, and they had a lot of respect for his business acumen, so amongst the Kleiner-Perkins people, they knew that they would

like to find a home for Bill Rastetter, they'd like to keep the whip in the family, so to speak, and they recommended to Bill that he look at IDEC. And I remember Bill coming down, we interviewed Bill down here in San Diego, and we were impressed, he has a PhD, he has a chemistry background, he's a very thoughtful businessman, he's pretty disciplined, straight. And then, of course, we had done this merger with Levy and Miller. I can't remember the name of their company.

JONES: Biotherapeutic Systems.

ROYSTON: Yeah, you know the whole thing. And I don't remember whether that was done before or after Rastetter, but I remember that one of the big issues that we had to decide was whether we'd close down one venue and consolidate, or whether we'd run both, and I remember the meeting where the Stanford people presented the reasons why everything should be up in Palo Alto, and we presented the reasons why it should be down here, and we couldn't agree, and it ended up that both places would continue to work but that San Diego would become the administrative headquarters, and Bill Rastetter would move down here. I think he wanted to leave the Bay Area. But after a number of years, it became clear that it was not, that there were too many inefficiencies and that company ought to be consolidated in one location, and at that point, Bill was already here, and the decision was made to close down Mountain View.

JONES: And did Richard Miller come down here?

ROYSTON: No. Richard Miller left the company. He did not want to move to San Diego and his wife was an oncologist at Stanford and Richard Miller became the founder of another company, which is now public, Pharmcyclics, another Kleiner-Perkins company in the Bay Area, and he's the CEO there.

JONES: Was Richard Miller at Stanford when you were there?

ROYSTON: Yes.

JONES: You knew him?

ROYSTON: I remember him. I was an intern and resident between '70 and '72, and then a postdoctoral fellow from '75 to '77, just prior to coming here, and then

Richard Miller overlapped with me, and then I don't remember, I think he was an intern while I was a resident.

JONES: Going back to Hybritech, how were the arrangements between Hybritech and the VA and Sam Halpern set up? Was that through you?

ROYSTON: Yeah. I introduced Sam Halpern to Hybritech. I introduced Sam Halpern into the field. I got him involved with monoclonal antibodies. When I wanted to get into imaging and therapy at the university, and he was at the VA, I asked Sam if he would collaborate with me and get involved with developing antibodies for imaging cancer, and he said he thought it would never work. And I said, 'Well, humor me. Let's try it, and prove either that it works or doesn't work.' Well, we started to plan some animal studies, and I still have the slides, I still show them, in which we injected radioactive antibodies into animals, you know, antibodies that were made against human tumors, and we used nude mice carrying the human tumors, and he was just blown away by how much specificity there was with this, in the nude mouse, of course, well in a mouse where the antibodies aren't reacting with any mouse tissues. The classical experiment that we did was, we injected a nude mouse. On one side we inject a human melanoma, on the other side we injected a human colon cancer. Then we injected anti-CEA, which reacts with colon cancer, and it lit up the colon cancer and not the melanoma, and vice versa, the antibody to melanoma lit up the melanoma. So, he was very impressed with that. It changed his career. You should interview Sam. Have you seen Sam?

JONES: No, I haven't. Is he still over there?

ROYSTON: Yeah. You should interview Sam because it changed his career, because until then, he working in some other aspect of imaging, but ever since he did that experiment with us, he spent the next ten years of his life just doing monoclonal antibody research.

JONES: And still?

ROYSTON: I don't know. Since I left there, I don't know how things have been going recently. I think he has been, but it's been a problem.

JONES: What was going on with the Board before the sale to Lilly? Somebody I talked hinted that a major shareholder wanted to liquidate and that was an important factor in selling the company to Lilly.

ROYSTON: Well, if there was a major shareholder who wanted to liquidate, that would be Henry Hillman, I'm guessing. You can always call him, 1-800-Hillman, and ask him, but I didn't know that at the time. But I was on the board at the time, and what I heard was that Eli Lilly would have an interest in Hybritech and that from Hybritech's perspective, if it was really going to get into pharmaceutical development, that it was going to take a lot more money than what was available, and that it could benefit from that kind of association. So, I personally know if that was a factor that Henry Hillman wanted to liquidate his shares. I just didn't know. I still don't. I think I've heard that rumor.

JONES: What were the discussions on the Board? Was this a unanimous decision that this would be a great thing?

ROYSTON: Yeah, I don't recall that anybody strongly opposed it. I don't think there was any strong opposition to it.

JONES: And you approved?

ROYSTON: Yeah, but in retrospect, I'm not sure that it was the right decision, in terms of Hybritech fulfilling its goals, but it was endorsed because we were told at the time that Eli Lilly would let Hybritech continue as a separate division, as Hybritech, and that it would have the support of Eli Lilly, but the culture does really change after this kind of merger or acquisition. The Lilly culture started taking hold and it was much more slow to respond to things, it became more bureaucratic, and people tended to leave.

JONES: When this happened, did you feel that you were losing something that was yours?

ROYSTON: No, I felt good about it, that it was going to have more support, more money available to develop the therapeutic side of the program, but I don't think that really came to be over time, but the feeling was really one of optimism, that this would be good for the company. So, I don't know. I don't know if you can say that we made a mistake or not. You know, Hybritech never was the same afterwards, and

eventually Eli Lilly sold Hybritech at a significant loss, to Beckman, so I don't feel good about the fact that it was never able to develop therapeutic antibodies, but then, you know, I've dealt with that, you know, with IDEC.

JONES: Well, what about the controversies at the VA and then at UCSD? I read about this stuff in the papers and I know about the broad issues, at the VA, you know, it was, how can you do both of these things…

ROYSTON: I know the university, you know, had some issues in terms of meetings about me and discussing how I could be involved in the company, and so forth, but I don't know if there were any official VA issues. There may have been, I know the NIH investigated me, somebody sent an anonymous letter, if that's what you're referring to. Somebody sent a letter to the National Cancer Institute suggesting that I'd done something improper or that there were improprieties related to my time at the University or the VA, and starting companies, but you know, it was always above board, it was investigated and I was exonerated. The NIH sent some people here, but really I found out that sent the investigators here primarily to investigate the burn people, Hansborough and somebody else, they were being investigated.

JONES: They were exonerated, too, right?

ROYSTON: Yeah, but while they were down here, they said, 'Well, why don't we do this Royston thing.' There was this anonymous letter that was sent in. We still don't know who sent that letter in.

JONES: Do you have an idea?

ROYSTON: Yeah, actually, it was somebody within the system, somebody at the University or the VA. And I got the letter under the Freedom of Information Act. It was sent to the Director of the NCI, Vince DaVita, but they spelled his name wrong, so I know it was not an oncologist, because they wouldn't have gotten the name spelled wrong. But it was somebody in the University system that really had a problem.

JONES: When you had this big success at Hybritech, did that cause problems for you?

ROYSTON: I think there were problems, jealousies, and stuff like that. Yeah, there were some problems, but I just had to ride them through. I think that when John Mendelsohn left UCSD to go to Memorial Hospital, he's now the President of MD Anderson, John Mendelsohn is, and the position of the Director of the Cancer Center was available, I found that I was not really taken seriously at the time because they felt uncomfortable about somebody who was so entrepreneurial, or involved with business, being involved at the University, so I had that kind of a role.

JONES: Did you want that position?

ROYSTON: Well, I don't know, I mean, at that time, I was never taken seriously. I thought about it, I guess. So, I can see that, you know, I had to pay a price there, not being considered. But I know there were some meetings held about me, and I think mainly University faculty, but I don't know exactly what you might be referring to besides that.

JONES: Well, there was a thing at the VA about how you weren't spending enough hours there.

ROYSTON: Yeah, there was article like that, wasn't there. That was all part of this investigation, I think. Was it something else?

JONES: Wasn't the investigation UCSD and IDEC, and this was about a year earlier at the VA.

ROYSTON: I can't remember. I think there was some accusation made about how I spent my time, but it was looked at, and everything was fine. You know, I wasn't different than anyone else in terms of spending time there. But I know there was a problem in the early days of Hybritech that the University faculty met and discussed how I was able to do all that, and what I'd wrong, and they found out that I hadn't done anything wrong, so there was nothing they could do. I mean, I had disclosed it all to the administration.

JONES: And at that time, this was pretty unusual.

ROYSTON: At that time it was unusual. Now, it's not unusual at all. Now it's the rule rather than the exception. Then it was the exception.

JONES: So, this was part of working the whole thing out, 'How do we deal with it?'

ROYSTON: That's why they say that pioneers have arrows shot at them, because when you pioneer something new, you're always going to have arrows shot at you, and I experienced that.

JONES: Had you ever thought about leaving the University and going to Hybritech?

ROYSTON: I never gave it any serious thought. Now and then, I have these, even right now, where I left the University to do this job, but I've always spent most of time in the non-profit world. The idea of running my own company seems very appealing sometimes, or, that is, starting a new company and running it and making it, like Irwin Jacobs has done with Qualcomm. That idea has appealed to me, but I've never really acted on it. I guess I've always been so committed to the non-profit world. Now, I do primarily administration here, trying to build this Center up. You know, this Center started with virtually nothing six years ago to where there's about twenty leading scientists here, and we're occupying 46,000 square feet of space in this building. So, this has been a real challenge, starting this thing, but it's been more rewarding, I think, than just staying at the University. The University is too bureaucratic for me. It takes too long to get things done. There are too many regulations, too many committees, too many, actually, I'm having a lot of committee meetings down here, unfortunately. I can see that bureaucracy is part of the price that you have to pay for getting larger, but there's too much of it at the University. It's a state institution, it's not going to have much autonomy within each cancer center, or what have you. So, there are other reasons as well, about how basic scientists and clinical scientists interact, but....So, this has been a much harder job, starting a non-profit center, I mean, being involved with the start-up of this compared to for-profit. It's harder to get people to support your activity on a philanthropic basis than, let's say, an investment basis.

JONES: Raising money is harder? But that's a lot of what you've done here, right?

ROYSTON: Right, well, developing programs here, recruiting, and now I'm going to embark on writing a grant to the National Cancer Institute, and that's a big undertaking. So yeah, I spend...I've thought about getting involved with my own company, you know, but I don't give it much serious thought. I'm pretty committed to this place, and I get my entrepreneurial, you know, my entrepreneurial thrills,

through my Forward Ventures association, and that's an interesting story, too, because I don't think there's any other venture capital firm that's run quite like ours where you have this part time person, which is me, involved in the scientific aspects, and then the day-to-day management is run by my partners, who are more business people. But I don't think you can find, I mean, you can find MDs who are venture capitalists, and I can name a bunch of them. I don't think you can find any other MD who spends as much time as I do in a university or a non- profit research institute, and also is involved in starting companies with a venture capital firm. That's pretty unique.

JONES: Well. I'd like to talk to you one more time, maybe we can talk about Forward Ventures because actually, I think a big part of this story, you know, all of these companies that have come out of Hybritech.

ROYSTON: There are other venture capital firms, you know. You know, Ted Green and Tim Wollaeger did Biovest, and Howard Birndorf had a pseudo, you know, his own money, I think he called it Birndorf Biotechnology.

JONES: Yeah, did he do anything besides Nanogen with that?

ROYSTON: I think that's primarily what he did, and I think it's just his own money, but…so, Ted Greene and Tim Wollaeger, Tim is now running Kingsbury Associates, so that's another venture capital group. Is that it?

JONES: I think so.

ROYSTON: Kevin Kinsella was separate. That's Avalon. H&Q is separate. They did Telios, Corvas, some others. So, H&Q Life Science Fund, that's Heinrichs, Avalon Ventures, Enterprise Partners, Jim Berglund, Drew Senyei, Kingsbury Associates, Sorrento Associates, and Forward Ventures.

JONES: These are San Diego…

ROYSTON: These are all San Diego based firms, yeah. Forward Ventures has a very good track record.

JONES: Before Hybritech, and before, you know, Link-a-Bit, Qualcomm, there really wasn't a venture capital community here.

ROYSTON: Yes. I remember when Hybritech was here, Link-a-Bit was here also, as I recall. It was about the same time. Yeah, they all followed. I don't know when Enterprise Partners started. I think they were around. Yeah, it's interesting to see San Diego grow into one of the top biotech centers of the world, and it's nice to be a part of it. You know, it's provided a lot of jobs. We didn't anticipate the decline of the defense industry, but really it's become sort of a real industry, with so many people trying to get into servicing the biotech industry. We've got a trade organization called BIOCOM, the CONNECT organization did a lot, does a lot in that area. But there are more biotech companies in San Diego than in any other city in the world.

JONES: More than the Bay Area and Boston?

ROYSTON: Yeah, because there are more cities in those areas. The Bay Area has multiple cities. I've chosen my words carefully. If you think about it, San Diego has the largest city area. San Francisco itself doesn't have any biotech companies, but you know, there's Palo Alto, Mountain View, San Jose, Alameda, Oakland, South San Francisco, each one of those is a city. It's not fair to say that, I mean, you want to take regions, and so we're probably third, and we have our first profitable, soon to be profitable company, with Agouron, with an FDA approved pharmaceutical. IDEC will probably prove to be the second this year, so I'm glad that if we're not the first, we're partly, at least, involved with the second. But you know, in retrospect, Hybritech was really instrumental. I was disappointed that it didn't get into therapeutics, but I'm happy that it was able to make a major contribution to medicine, and that would be the PSA. It really revolutionized cancer care for men, with that test.

JONES: Who was involved, primarily, with developing that?

ROYSTON: I was in the room and took the minutes when we said we were going to do PSA. I think Gary David gets the credit for that.

JONES: Because it was using a TANDEM assay?

ROYSTON: Yeah, and I remember him saying, 'You know, I think I can get the PSA antigen out of Roswell Park,' where it was just described in a paper. And so, they licensed it and then we had to use it to make antibodies and make two sets of

antibodies and develop it as a TANDEM test, then once we got it working and testing people's blood and starting to see how it correlated, that it was positive in patients with prostate cancer and negative in normal males, and starting to see positive tests in males before they diagnosed with prostate cancer, and finding out that we could diagnose it. It became the first major screening test for cancer. CEA is always a screening test for colon cancer, after you have the disease, but too many false positives before you have the disease. There are very few false positives in prostate cancer. I mean, there are some, but it's approved as a screening test. So, that was a major contribution. So, I'm happy that Hybritech did that, of course. The other thing that I'm really happy to be a part of is, of course I'm happy to be a part of the biotech industry, but you know, we've created a lot of job in San Diego, made San Diego a better place, still making it a clean business environment, there's no manufacturing pollution. It's kind of like the wireless information technology, it's very clean. Biotech's pretty clean. It just needs a lot of water.

JONES: well, what do you see for the future? I mean, now that there are pharmaceutical products, there is talk that manufacturing might be a problem. What do you think is going to happen?

ROYSTON: Yeah, people find that manufacturing is cheaper in other places, like Puerto Rico, or somewhere offshore, so I do see that kind of shifting, but no, I think there is going to be continued growth in the biotech industry in San Diego. There are still lots of opportunities and there will be a lot more products coming out of the existing companies. There will be some consolidation, and some companies won't make it, but I think it's a pretty healthy industry, and it's going to get better.

JONES: Who developed the hollow fiber technology for producing antibodies?

ROYSTON: I don't know who developed that. I know that Unisyn here in San Diego, they moved to Boston, was very active in that area. I think it's Dow, wasn't it Dow-Corning?

JONES: I'm not sure. I'm trying to find out.

ROYSTON: Richard Miller might know the answer to that, up at Pharmacylics. Because he was pretty involved in looking at the whole hollow fiber technology for growing antibodies.

JONES: And that pretty much became the standard?

ROYSTON: Yeah, well no, now you make them with fermenter tanks. But small amounts of antibodies can be made with hollow fiber, when I say small, I mean medium amounts.

JONES: But it's not like in the early days at Hybritech where you used thirty thousand mice.

ROYSTON: Yeah, but hollow fiber, Unisyn Technologies, I used to be on the Board of that company, before it left San Diego and went to the Boston area. One of the major stockholders in Unisyn was Synbiotics, the company you mentioned. It was a spin-off from Synbiotics. But I think Dow started that whole hollow fiber thing.

JONES: Listen, when I'm looking for published results of clinical trials conducted by Hybritech and IDEC, what are some the names I should look for?

ROYSTON: Well, for the clinical trials for IDEC, you mean names for searching?

JONES: Yes.

ROYSTON: A lot of those trials have university or academic investigators on them, but usually the name Grillo would be on those papers, Tony Grillo.

JONES: How do you spell?

ROYSTON: G-R-I-L-L-O. He's the medical director at IDEC. His name appears on most of those papers. Also Christie White. She used to work here, and is now a medical director at IDEC. Christine White. With regard to Hybritech, you mean which clinical trials, like PSA?

JONES: No, for imaging and therapeutics.

ROYSTON: Oh, Sam Halpern and there's a guy at MD Anderson, Murray, Ed Murray, I think, Bob Murray? Bill? The last name is Murray

INTERVIEWEE: **Ivor Royston**

INTERVIEWER: **Mark Jones, PhD**

INTERVIEW: **Part 3 of 3**

DATE: **October 31, 1997**

LOCATION: **San Diego, California**

ROYSTON: ...to have an approved product finally, after all these years. So, it took from 1986, it took eleven years, from the idea, from the founding, the idea was before that, to have a final product. Even though I told all of the venture capitalists that it would take only four or five years.

JONES: Eleven years is not a long time.

ROYSTON: Right. Actually, the product that's going to be marketed was only developed over the past five or six years, because they shifted gears. So, actually what I had suggested for the founding of IDEC actually did not materialize. It came from within the company.

JONES: But it was still a monoclonal product.

ROYSTON: Right, it was a monoclonal product. The idea was to have a monoclonal product for treating lymphoma, cancer of the lymph system, and that's what they have. It will be the first revolutionary new product for the treatment of lymphoma. So, IDEC in 1997, when we expect they will actually get an approval this year, I suppose it's going to have to be in the next two months then, final approval, just pending manufacturing and labeling issues. That product, think about it, 1997, nineteen years after the founding of Hybritech, 1978, when I said to Brook Byers, 'You know, I think we can use monoclonal antibodies to treat cancer," and it's with IDEC, the second company that that has now come to fruition, but it took nineteen years for the first monoclonal antibody to be approved by the FDA to treat cancer.

JONES: Well, it's a complex problem, a very difficult thing.

ROYSTON: But it happened, so that dream became a reality, will become a reality.

JONES: What were you doing in the late '80s? You were still at the university.

ROYSTON: Yeah, and then I was going through a lot of soul searching, and a lot of politics, as there were a lot of changes going on in the university. John Mendelsohn, the director, left to go to Sloan-Kettering, and I was getting, you know, doing more stuff, and I was on more committees, and we were trying to deal with issues like building, unifying the UCSD Cancer Center in La Jolla, and all of this activity got me very frustrated when I saw how slow things were moving along, and then how plans that we'd be working on for over a year had gotten derailed and cancelled, and I got fed up. And then 1990, I saw the opportunity when some friends of mine met, I mean you could feel the frustration, I mean my friends knew I was getting frustrated and sort of unhappy with the bureaucracy and how things were developing at UCSD. They said, 'You know, maybe we should try to start a new cancer center.' Because they felt that there was no really good cancer center in San Diego, and that UCSD wasn't going to provide it, and I was more inclined to consider that, and that led to the birth of this center. And in 1990, I made the decision to do it. And I transferred my grants from UCSD to here. So, in December of 1990, we started this Cancer Center. Now at the same time in 1990, I was just starting to do, also dabble in more venture capital activities.

JONES: Now there were some other people leaving UCSD at the time, right?

ROYSTON: Ray Taetle left before me. And afterwards more people left after I left. After I left, then subsequently, Robert Parker left, and Mark Green left. Mark Green was the guy who became the Cancer Center director after John Mendelsohn left, and a whole bunch of people left.

JONES: Had you started working with gene therapies before coming here?

ROYSTON: No, only after coming here.

JONES: So, your research at the Cancer Center there was still....

ROYSTON: Yeah, it was still monoclonal antibody-based research, applications of monoclonal antibodies to cancer. I brought that here, that's right.

JONES: At the time, an important issue was the NIH designation of the cancer center, a regional cancer center?

ROYSTON: You mean here?

JONES: In San Diego.

ROYSTON: UCSD got, while I was there, received the designation of an NCI, designated clinical cancer center. That happened while I was there in the mid-80s, or early 80s.

JONES: There is a competition for this?

ROYSTON: It's a competitive thing, yeah, and now I want to do something similar here, but, yeah, they've had that for quite a while.

JONES: Who were the friends you mentioned who sort of planted this idea?

ROYSTON: My friend was Tom Shifton, the chairman of our board here. I met him when I first arrived at UCSD in 1977, because he was just finishing his fellowship. He was a postdoctoral fellow in oncology. So, I just started on the faculty, and he was a postdoctoral fellow just a year junior, even though he was probably about my age, or maybe a few years younger. So, after he finished there, he went abroad for a year, he worked for a year, he came back here and went into private practice. And he got also thinking, started thinking about the cancer center issues, and just thought that UCSD was not providing the kind of leadership in cancer research and cancer care that he expected from a city like San Diego. And he thought that there were other alternatives. And then Alan Goodman was the other person. So, Tom called me, and said to me one day, 'Look, I know you're interested, you're not happy with the university, and you're thinking about…' Oh yeah, I remember, I must have told him that I had presented a proposal to the chancellor to build a new biotechnology research institute. That's interesting, we can come back to that. Because that fits into the Hybritech and IDEC thing. I thought that, yeah, I'll come back to that. I forgot about it myself. I just reminded myself. So, he said, 'I know you've been thinking about alternatives to what you're doing at UCSD. I'd like you to meet somebody, a doctor here in San Diego who's just lost his son to leukemia,' and was not happy that San Diego did not provide the kind of services that he wanted, because he had to take his son either to Seattle or Stanford. So, we ultimately had this fateful, pivotal lunch at Busalacchi's [Buslacchi's Ristorante; traditional Sicilian cuisine; 3683 Fifth Ave.] which, where we together talked about cancer centers, and each for their own reasons saying, you know, 'We need more than what we have.' For totally different

reasons, Tom Shipton, Alan Goodman, and myself, but we all came to the same conclusion.

JONES: What was Tom Shipton's reason?

ROYSTON: He just felt that the UCSD Cancer Center wasn't really serving the clinical needs of the community, that it was not clinically oriented, but more basic research oriented, which is probably true, and I was more interested in a more entrepreneurial environment, and one in which there was less bureaucracy and able to move more quickly on things. And so, Alan Goodman said, 'Look, I have this big office building across from Sharp Hospital,' he was a thoracic surgeon at Sharp, and Tom Shipton was now practicing also across from Sharp. But Al Goodman said, 'Look, I own all of these office buildings, and you know, they're for sale, and as soon as I get the money, I'm going to give you guys a lot of money.' He's never done that, but that pledge, plus the fact that we all signed a credit line, and plus the fact that I was able to get Chris McKellar, the real estate developer here to build some labs in this building that we could lease back without putting any cash down, all those things came together, and so we started this cancer center. So we essentially started this cancer center, this is interesting because this is much harder than the for-profits, where you can bring in investors and tell them, 'Look, you might make a lot of money.' Here, no one's making any money. And this is much harder. But basically, we started this cancer center within about, I can show you the original space, in this corner of the building -- there was another tenant in here -- with no money, no cash, we had a credit line that we all signed on personally, a pledge from Dr. Goodman that when his buildings would be sold, he'd put this thing in. You probably remember that we went into a real estate depression here, so those building never sold. I transferred my grants from UCSD and brought some people over here, and that's how we started. And today, 1997, six years later, it will be seven years in December, yeah, that's amazing, seven years later, you know, we have about 100 employees, about 20 principal investigators, and we occupy most of this building. And that, in retrospect, is a pretty remarkable achievement, too, in a time when we were actually in a depression in San Diego. And that was much harder than any for-profit.

JONES: But you've been successful in raising money.

ROYSTON: Well, Mr. Kimmel's gift was very important. He made a naming gift that really helped us out a lot. We named the Cancer Center after him. Mr. Kimmel is the chairman of Judson-York Clothing, founder and chief executive of Judson-York, a very, very successful clothing company which makes clothing for women, primarily, and you know, I was introduced to him, and he was willing to get involved, and made the gift. He's on the Forbes 400 and he's got, his net worth has increased substantially, his company's very successful, it's worth maybe a billion dollars right now.

JONES: How did you meet him?

ROYSTON: Through a mutual friend. Somebody came to visit us, who's daughter was dying of cancer, and he was very impressed with what we were trying to do, and then his daughter eventually died. There was nothing we could do to help, but we developed a relationship and he called me one day and he said, 'Look, I want you to meet an old friend of mine.' That was Mr. Kimmel. That's how it happened. It's amazing, isn't it? You never know what's going to turn up. So, Mr. Kimmel had never been to San Diego. He's been here two times now. The Busalacchi, to commemorate that dinner in which the idea of developing this cancer center emerged, we had our first major fund-raising gala event last summer, and for that event Busalacchi donated all of his time and underwrote the entire dinner. And I have pictures back here to commemorate that dinner, in the hallway, of the gala, and Busalacchi underwrote that in commemoration, so it was very nice. So, that was, you know, I was still trying to build the cancer center, and I've got a parking lot here, the grass is all gone now, but we've got options on the land around here, and what's confronting me now is the development of this little park as a little mini-campus for ourselves. Johnson & Johnson is going to build their basic science research center next to us. Just to get back, though, before I left, while I was getting frustrated, I was looking for something, something new, I was getting pretty antsy with the leadership at the university and the Cancer Center and the bureaucracy, and I just wanted to do something on my own, and I knew the chancellor quite well, and I said, 'You know, I like being affiliated with the university, but I'd like to start my own biotechnology research center or something like that.' Something like what Gallo has done subsequently now in Baltimore, and if the university would throw in the land, we could build it on the university, I 'd met some real estate developers that were

interested in getting involved, and I put a whole bunch of proposals to show the university, but it just didn't go anywhere.

JONES: And what kind of work did you envision would take place there?

ROYSTON: At that time, the vision wasn't that it would be cancer research, because we already had a cancer center. But it would be basic, I'm not sure thinking back then, exactly, both basic and translational research, I mean it would be a focus on cancer, it would have been affiliated with the Cancer Center, sort of, that's how I envisioned it, but it's been so long, I haven't thought about it, it probably wasn't, I haven't even thought of it until just now. Anyway, the point I was trying to make was that I was going through this active thought process at the time, trying to come up with something new that I might want to, that I'd be more in control of, and then when these guys came along and said, 'Why don't we just do a new cancer center,' and you know, UCSD is not really doing the job, and it meant, well, competing with UCSD, and leaving UCSD, I just eventually decided to do that.

JONES: And would you say that not getting anywhere with biotechnology research institute over there contributed?

ROYSTON: Sure, because if something had happened, I might have been willing to follow it along. Maybe it was good that it didn't happen. Well, I was aware that there are independent institutes that are affiliated with the university, that can build on the university. There's a Mexican, Latin, Institute of the Americas, something like that, that is independent, so I knew that those things were possible. I saw the possibility of building up some kind of new structure that could be maybe its own organized research unit, like a Scripps Oceanographic Institute, or a new center of some kind. I was frustrated, just being, just with the whole process, being sort of under the thumb of the Dean, and whatever their issues were. It's a great place if you just want to have your own lab and do your own research, but if you want to create something, it's not really very good. So, it's much better here, where, you know, I can be involved in creating, you know, a new center. So I like the start-up process. I have to admit, doing the administration is not what I really enjoy, running this thing, although, I mean, as we grow, there are so many more administrative issues. And I don't have a chief operating officer, which I'm trying to recruit for, so I'm doing everything, and I'm not doing it well. I don't like the day-to-day administration.

JONES: Where are you recruiting?

ROYSTON: We have a headhunter, a search firm, and we're recruiting nationally. And we do have a lot of resumes.

JONES: An industry person?

ROYSTON: No, the ideal person is someone who comes out of a non-profit research environment that has good financial skills and interpersonal skills. You know, someone would could really watch the money and be both a chief operating officer and chief financial officer.

JONES: So, that would free you up to do….?

ROYSTON: Yeah, I'm trying to work on a major grant now, and I think it's started, and that's why Bonnie left a message, can you meet, because after this meeting, I have to be in the Bay Area next week, I think, after next week, I'm not going to have any more meetings with anybody. I need to lock myself up here, and I've got a major grant that I need to write, that I have to work on myself. So, that's what I'm going to work on.

The other things since IDEC. I was on the board of IDEC for a number of years. I did go off the board in the '90s sometime, early '90s, right after their IPO, I think it was '91. Maybe I stayed on the board until '92 or '93. But I eventually went off the board. But the other thing that is interesting is that I started to, while I was at the university, I should say, you know, I had done Hybritech, and then IDEC, and then IDEC was getting more well-known, and what happens over the years, it's been, let's take 1988, '89, we're talking ten years after Hybritech, right?

Hybritech's already acquired by Eli Lilly, and what happens is, it's much more acceptable now, and more the norm, for university professors now to be involved with their companies. I said this once before, if you're not involved with a company, often time you often wonder, well, that guy's really not that good, because most people are involved with companies, one way or another, as a consultant or as a founder, whatever. So, what happened was, I started getting calls, from all kinds of scientists all over this town, 'Can you help me? I think I have an idea for a company, what should I do?' I would get all of these calls, so I used to refer them to, I used to say, 'You know, you have to call a venture capitalist, you know, you can call these

guys in San Francisco or wherever.' And then people started saying, you know, 'Where should I invest my money?' And then it dawned on me, you know, I like business, I've always had an interest in business. It wasn't my primary occupation, or my primary interest, but I l always liked business. I enjoyed being around business people when I was involved with Hybritech and IDEC. I enjoyed a different way of thinking about problems. The fact that my primary interest here was the rapid translation of laboratory findings into clinical applications, that sort of went along with the commercialization of products. I decided, well, and I had some money from Hybritech. I had some money that I'd like to invest, so I said, 'Well, I'll put a little fund together, a little venture capital fund,' and I invested in it and put in half the money, and then all of a sudden I had friends and family and all kinds of interest when they heard what I was doing, and they said, 'Well, we want to invest, too.'

JONES: A lot of people trusted your judgment.

ROYSTON: Yeah, but it wasn't a big fund, I mean, the whole thing turned out to be about one and a half million dollars. So, I started, and sure enough, I got a call from a university professor in 1990. Ted Friedmann, who made the first call? Ted Friedmann, Rusty Gage? They called me and said, 'We want to start a company.' So, I go over and look at them, and they tell me that they want to develop a cure for Parkinson's Disease using gene therapy. That's when I first got introduced, first started really thinking about gene therapy, 1990. God, I think it's been around forever, it's not even a decade yet. And I got real interested in their idea, and all of a sudden, I realized there were cancer applications. So, I threw that in. I said, 'Look, we shouldn't do just Parkinson's Disease, Alzheimer's, whatever, CNS disease, let's throw in cancer, make it a little broader, same technology, same core technology.' And they liked that idea, and I started working on it. And that's where I met my partner, now, just to let you know, I'm now a general partner in a venture fund called Forward Ventures, but I met, what happened is, one of the guys who had called me, he or the other person had called Ventana, another venture capital firm in San Diego, and this young guy, not young, but I mean junior guy, Stan Fleming, shows up one day to meet me when I'm there.

JONES: He was with Ventana?

ROYSTON: Yeah, he was an associate of Ventana. Stan Fleming shows up because they got a call to learn more about their technology, then he finds out that I'm

interested and all of a sudden, he gets interested in it. But to make a long story short, and because I'm not a professional venture capitalist, this was just like a hobby for me, I was just sort of dabbling, but with other people's money, half of it was my money, I said, 'You know, I'd really like to get involved, I'd really like to put some money in this, like $250,000, so Stan Fleming says, 'Look, why don't we just do this together,' or I may have said that, you know, 'Why don't we do this together, why don't we each put in $250,000, we'll seed this thing.' And that's what happened. So we seeded it, met with these guys in the evenings, worked on business plans. I was still at the university. That means it was before December of 1990. It was sort of '89-'90. So, maybe I'm a little off on the years, because I know that I was there, I know that I started that process before I came here. So, all these things are going on simultaneously, getting a little venture capital activity. Maybe I was sort of searching for something new to do, trying different things. So, I'd meet with these guys in the evening, I was on the boards, we put this thing together, and over time, you know, we were writing the business plan, recruited one of my associates Bob Sobol who works here. He's downstairs, actually, if you wanted to interview him. Bob Sobol was a founder of IDEC. I can't do everything, so I usually try to recruit in people that can help out in one way or another. I said, 'Bob, do you want to get involved with this?' And when he saw the cancer piece that we came up with, Bob got real excited about it, got involved in that, in really putting that together, and really writing the business plan. And so what happened was, that thing took off, and we got Kleiner-Perkins to invest, and then, eventually, it was actually acquired, within a year, by Somatix.

JONES: So, this is Genesys, right?

ROYSTON: That was Genesys Therapeutics. That's the name of the company Genesys Therapeutics. So here, my first investment as a venture capitalist, and as sort of a quasi-co-founder, because we came up with the cancer applications, so this turned out, the total investment probably with Kleiner-Perkins was, like, a couple, a few million dollars altogether, it was acquired within a year by Somatix for a stock value of $30 million. It's gone down, it's lost a lot of money since then.

JONES: So this investment actually preceded Forward Ventures?

ROYSTON: That was Forward Ventures. That was the beginning of Forward Ventures, with me. Now, after we did all that, Stan Fleming realized he didn't have any future at Ventana, they were a schlocky operation. So -- don't quote me -- I'm off

the record on that. That can't go into print. So, Stan and I, we worked well together on this, he's an MBA guy, you know, he's not a scientist. And I knew that my passion was what I'm doing here, the research. This was just a side thing for me. And I knew that I couldn't do more Genesys Therapeutics, things like that, without, in a systematic way, without having a partner, an MBA. And he said, 'Why don't we do this together, professionally.' 'I'll help put this thing together,' Stan said, 'as a professional venture capital firm.' He'll essentially run it, as the managing partner, so to speak, 'we'll be partners, and we'll raise money.' I said, 'that's sounds like a good idea,' and I enjoyed working with him, I mean, we're very different personalities, very, very different. He's compulsive about things, he loves to document everything and write detailed letters and notes to the file, and everything with me is verbal. With him, it's all done, and he's very compulsive about everything being in writing, very responsive in terms of communicating with other people, and investor relations, as it subsequently turned out to be, but he didn't have, I don't think, the intution or the scientific background that I had. So, anyway, we complemented each other. We weren't two Harvard MBAs, like Ted Greene and Tim Wollaeger, who tried it and clashed all the time. We had complementary skills and we didn't clash. We had totally different... So I said, 'OK, that's sounds like a great idea.' I had worked with him on Genesys Therapeutics, and I enjoyed the interaction and everything worked out fine, and so I said, 'OK, let's do that.' So, without any salary, Stan quit Ventana. He quit Ventana and spent all of his time trying to put a fund together with me and raise money for Forward Ventures, II -- which it turned out to be. But what I did in recognizing that this might turn into a more professional fund, I started making investments to invest that one and a half million dollars more rapidly in things that were already up and running, because I had so many other people coming to me all the time, PRIZM and IXSYS, and people saying, "OK, how would like to invest in this?' So, I started looking at things in a more passive way, and making investments so that I could then focus my energy more on what I would say is Forward II. And that's what happened. Stan put together documents and proposals, the kinds of stuff that could be used to raise money from other investors, and together we raised about twelve and a half million dollars from various investors institutional investors like AT&T pension plan, American Cyanamid, and a couple of venture capital firms, Sequoia Capital and Asset Management.

JONES: Did you have any problem doing that? You're a physician-researcher....

ROYSTON: Well, we tried to present that as a big plus. This was unique, you know, I was at Hybritech and IDEC.

JONES: So you already had a lot of name recognition from those things?

ROYSTON: Right. And now Genesys Therapeutics that we'd put together, so we had a track record. So, we raised that and we invested that. That was raised in 1992, 1993 time-frame, and it was all invested by now, 1996. And now Forward Ventures has raised a third fund, Forward Ventures III, and now has a third partner, Jeff Sollender, and just closed on a forty-two million dollar fund. So, that's growing, too. On the one hand, the third partner makes it a little bit easier for me, on the other hand, there is, you know, like, I have a meeting that I go to there every Monday morning, and then periodic meetings. My role is really more one of scientific evaluation. So, I get a lot of that, and now that Forward Ventures is known, and Forward Ventures has been successful, and Forward Ventures II had a very good success, a very good return, rate of return, Forward I, the hobby fund as I call it, didn't do all that well compared to other venture capital firms. I mean it was not a stellar success from a financial point of view.

JONES: Even with Genesys?

ROYSTON: Well, if you had sold it right away, but over time it went down. I mean, it has, in venture capital jargon, Forward Ventures I probably had, since its beginning in 1990 or 1989 until now, you would equate it with a twenty percent annual rate of return. Which is good, it's better than conventional, something conventional, except that, you know, over that time period, that's pretty good, but Forward Ventures II, in the time frame between 1993 and 1996, I believe was the time frame, had a much better track record of having between sixty and seventy percent rate of return because there was one company that was started that was extremely successful. It might even have been more successful than Hybritech was, and that was Triangle Pharmaceuticals, in Triangle Park, North Carolina. That was incubated in our offices, and one of the founders was a UCSD professor, Karl Hostetler, who also was a co-founder of Vical.

JONES: Dennis Carson and Doug Richman were also involved?

ROYSTON: Yes. And it's a company that's involved with anti-virals and HIV. I was instrumental in bringing on the CEO of Triangle who, which was the main reason why it's so successful because the CEO of Triangle Pharmaceuticals was formerly the head of worldwide research for Burroughs-Wellcome, and was somebody that I had worked with between 1972 and 1975 when I was at the NIH. I had read in the paper, when I knew that we, Forward Ventures was working on an anti-viral company with Karl Hostetler's technology, and Dennis Carson's.

JONES: It was called Procal at that point?

ROYSTON: That's right. Boy, how'd you get all of this information?

JONES: I talked to those guys. I haven't talked to Hostetler.

ROYSTON: I'll come back to Hostetler. We're working on that, and then I read in the newspaper that Burroughs-Wellcome was going to be acquired by Glaxo, and I knew that Dave Barry was the head of research for Burroughs-Wellcome, so I remember, I was in the room with Forward Ventures, and I said, 'Look, what's going to make this company go is we've got to get a good CEO. Why don't I call, I said, 'I've got the Wall Street Journal, it says here that Burroughs-Wellcome has just been bought by Glaxo. Maybe these guys don't want to go to Glaxo. Why don't we, let me call Dave Barry, and see what's going on, because he'd be an ideal candidate.' I hadn't seen him in twenty years. So, I called him and I did get through to him, and he thought it was a great idea. I said, 'Are you going to Glaxo?' He said, 'Hell no, I'm not going to Glaxo. I tried to buy Burroughs-Wellcome. I'm really pissed off.' And so I said, 'Would you mind considering, I'm involved with a venture capital firm, Dave, and could stop by San Diego? We've got this little start-up out here. Maybe you'd like to be the CEO of this company here.' And his answer was, 'Well, I've got to go to London,' and he's in Triangle Park -- 'but I think I can stop by San Diego on the way to London.' So he did. I met him at the airport, showed the thing, and he got real interested. A few weeks later he said, I'll do it. Not only did he say 'I'll do it,' he said wanted to invest his own money. Very rarely do you find that situation. So Triangle became very successful because that's the key thing. If you can get the right technology with the right management, that's what makes a company successful. It's the people, it's not the technology. Everybody says this. It's probably true. I see it over and over again. If I had a choice between technology and management, I'd rather invest in the people because people find technology. The people that know

how to make things happen. As was the case with Triangle. So, Triangle was very successful. It grew very quickly, very rapidly, went public quickly, and I think it may have gone public more quickly than Hybritech, and achieved a greater, well, I don't know what the overall return on the company has been.

JONES: But it also didn't start from scratch, I mean, it had drug candidates, right?

ROYSTON: Yeah, that's right. Karl Hostetler is interesting, to get back to him, because, you know, he's been, whereas I may have been involved early on in this thing, I certainly don't consider myself the most successful beneficiary. What I'm trying to say is, I don't think I made more money that anybody else. I think other people have done better financially than myself. For example, Howard is an example of that, or Karl Hostetler, because he was a founder of Vical and now Triangle, Triangle's been very successful, so I find it amusing that Karl Hostetler is on sabbatical this year, and he's at the UCLA film school, learning to be a producer. He's in Los Angeles. I think he comes down here one day a week, but he has an apartment in Los Angeles now, and he's studying how to make films.

JONES: Well, you had a production company. Did you do that just for fun?

ROYSTON: But I didn't go to school. It was called Pacific West Entertainment Group, and it was, that was just a fun thing for me to be involved with, and I was not that actively involved. I was sort of passively involved. I had a close friend who was very interested in the entertainment business, and Dennis Carlo got interested in it, so the three of us hooked up, and we decided to throw in some money, and we lost a ton of money in that. What happened is, my friend Neal, who put this all together, Neal Schulman, was the one who wrote Doc Hollywood, and he was successful with that project, but Doc Hollywood was not part of our group. It was an independent thing, not part of Pacific West Entertainment Group. But Pacific West Entertainment Group, we took a credit line out, we all signed on it with the First National Bank here, and we hired, we opened an office in Los Angeles, we hired a woman that Neal referred to us from Atlanta who used to be the head of video for Turner Broadcasting, and she flew out here to run our office. This was in the late '8os.And we made some money on our first project. We had the rights to the Mel Fisher story, called Dreams of Gold, and that was made as a TV movie, and Pacific WestEntertainment Group got a credit and got some money out of that, and we reinvested all that money, and we thought that instead of going into making motion

pictures for the theatre, we'd take the easy way out. We'd make a motion picture, but it would be a B- movie designed to be primarily released through video. Because of the overseas market, we were convinced that we could get all of our money back just in overseas sales, and then there would be a lot of profit in a year. So, Connie, who ran our office, got involved with putting the deal together to make this movie called Soultaker, which we produced and paid for. It cost about $300,000 to make it. Again, I was not actively involved. I was quite passive here, because we had a full-time person working for us. We had a distribution deal with this company, where they would keep 20% and they would return 80% to us, because we paid for the movie, and we got this new director out of the UCLA film school, who really liked the project, to do it very cheap. Everything was done very cheap. And I have to admit that after it was made, only $300,000, there were some overruns, maybe $400,000, I tell you, it looked like a million-dollar movie. It was actually quite good for that money. It was a thriller. It was a science fiction thriller called Soul Taker. It's about this guy who crashes his car and his soul leaves his body before, you know, the soul is running away. It was actually not too bad. It starred Emilio Estevez' brother, Charlie Sheen's brother. It was actually quite good, because not only did it do well and sold overseas quite well, it actually went to theatres here, on a couple of screens, and it got reasonable reviews, and I have seen it at Blockbuster. It actually sold quite well, but we lost all of our money because what we didn't realize is that most people in Hollywood are dishonest. And what happened is that distribution company that we made a deal with stole our money. They sold the tapes, the videotapes, but they never gave us any money, they kept it. And they knew we were down here, and they knew they could just rip us off. They were really quite dishonest. So, we had to file a lawsuit against them, and that used up all our capital reserves, and one of our partners went bankrupt, because he's in the real estate business, and it was a big, big mess, and we just lost a ton of money. I lost a lot of money, even though we could have made money because it was a successful movie. I'm still dealing with that right now, because we reached a settlement with them out of court, we wouldn't go to trial, ...?... and they agreed to pay us back, $400,000 over some period of time, and then they stopped paying us, and we have to go back and do something again. It's still going on, we had a court judgment against them. So, we got out of that business. You cannot do this passively, you cannot do it from San Diego. You have to be in the business, making movies, or not. You don't dabble. So, we learned that lesson the hard way, but you know, we're naive, we think that people are honest like ourselves, and there are a lot of crooks out there. Only five percent of the movie

business is honest, so you have to know which five percent they are. So, we've been all around the block. So, it's interesting that Karl now is going to make movies. The first thing I did was introduce Karl to my friend Neal, who did Doc Hollywood, so they met each other. Karl just now brought Forward Ventures now another idea that he wants to form a new company, a third company, so my partner Stan Fleming is working on it

JONES: Were you involved in bringing Hixson from Amgen?

ROYSTON: Well, we were involved in getting Hixson into Genesys Therapeutics. Hixson left Amgen when he was not elected to be the CEO. He was the president of Amgen, reporting to George Rathman, who was the CEO. When George Rathman left to start, I think it was called ICOS? -- whatever -- they had to decide on a new CEO at Amgen, and it was between Gordon Binder, the CFO, or Harry Hixson, the president, and he grew up through manufacturing, and, well, science, too, he's a scientist. And they chose the other guy, they chose Gordon Binder to be CEO of Amgen, and so Hixson left. He made a ton of money with his stock options, at least $50 million, I'm sure, and he decided to move to La Jolla, so when we heard that, we went right after him to see if he wanted to be the president of Genesys Therapeutics, and he said yes, but then he did a switch on us, because as soon as we started working with him and agreed to be the president, he told us that he was not going to continue as the president, that it would not fit in with his new life style, and therefore, I think he may have worked against us, because he was the one that really pushed for the idea of merging this company with Somatix, because by doing that he was going then to become Chairman of the Board, a paid chairman of the board of Somatix, and would not have to work as hard. Anyway, that's the way we went. I don't know what would have happened. So, we were involved in recruiting Hixson to Genesys Therapeutics once we heard that he was moving to La Jolla.

JONES: Was Inder Verma also involved in Genesys?

ROYSTON: What we did when the first two founders came to see us, that's Ted Friedmann and Rusty Gage, and were putting programs together, adding the cancer piece, we came up with the idea, I'm not sure exactly how we came up with it, we came up with the idea that we should get Inder Verma involved with the company, and I talked Inder Verma into joining the company. He was a consultant to Viagene, was not happy as a consultant to Viagene. Viagene is the company that ultimately

got bought by Chiron, and so he agreed to become sort of a founder. I mean, he wasn't really a founder, he was a second generation founder, and also so we could go into cancer. You know, Inder's lab was very involved with that, with this area of research. So, we worked with him, and also we wanted to license his patents. That's what happened. We recognized as we were doing our due diligence on Genesys, we realized that there were some patents that the Salk had that would be very beneficial to us, and one thing led to another, and we realized that it would be very beneficial if we could get Inder Verma and the Salk patents to be licensed to Genesys Therapeutics. That's what happened, and we made Inder Verma essentially a co-founder, months later. And then that group, a very stellar group, and of course that was very appealing to Somatix and the founder of Somatix was Mulligan, who's a good friend of Inder Verma's. They knew each other quite well.

JONES: So, that was a key part…

ROYSTON: Yeah, that was also a key part to getting together. Maybe the core part.

JONES: Was the first company that Ted Friedmann had been a founder of?

ROYSTON: I think so, yes.

JONES: Has he done stuff since?

ROYSTON: I don't think so. He may be a consultant to some things, but I don't think he's been a founder. Inder Verma's been a founder of Signal, so was Rust Gage, with Harry Hixson. Harry Hixson got along well with those guys. I was not happy with the way Somatix went. I don't want to go into it really here, but I wasn't happy. After the merger was completed, I went on the board of Somatix myself, it was Harry and myself, and their guys, and I was not pleased with the way things developed. I resigned after a while.

JONES: What about the other Forward Venture companies here in San Diego. There have been a number of them, right? MitoKor?

ROYSTON: The one's in San Diego from Forward II are Mitokor, First Dental Health. Some of them moved out of San Diego. They started in San Diego and moved away.

JONES: Is Dynavax III?

ROYSTON: Dynavax is III, a small piece.

JONES: Combichem?

ROYSTON: Yes, Combichem. That's a big one in Forward II. Yeah, that was with Scripps Research Institute. They're going to go public soon, hopefully. Combichem and MitoKor are the major holdings, in addition to Triangle, that is. Triangle, by the way, we tried to start to here, and Dave Barry was willing to move here, but as soon as it was learned that Dave Barry was going to become CEO of this company, all of the other guys at Burroughs- Wellcome wanted to leave and join the company. Well, all of a sudden, you had…side ends Combichem and Mitokor were major company opportunities.

JONES: How did you make those connections?

ROYSTON: Combichem was made with Scripps Research Institute. That was made via, I mentioned that Sequoia Capital was a limited partner of Forward Ventures, and somebody, it may have been Richard Lerner, somebody mentioned, was at a meeting and bumped into one of these Sequoia Capital guys, and mentioned that there was some interesting technology at the Scripps Research Institutes that might be the basis of a new company, and we got a call from Sequoia asking us if we could look into it, which we did, and we agreed that it was. So, that's how that happened, and so it was introduced to us from Sequoia. The other company, MitoKor, that was presented to us by the group that was raising money. Initially, we rejected it because we thought it was too speculative. We said we wanted a little bit more date. I mean, it was a great idea, but, you know, we just weren't comfortable, the risk tolerance was a little bit, we found it too risky, so we said, 'We'd like to get more data.' Well, El Dorado ventures, who I'd never heard of before, and who obviously must be smarter than us, and decided to invest in it, and they were able to get the data we were asking for, and they came back a second time, and that time we went in, so it was sort of a second round.

JONES: Can you tell me about the research that you've done here at this center, what you started out with and where you've gotten to?

ROYSTON: Well, we have a lot, we have essentially twenty principal investigators here now, and so we have a lot of different research programs here. But we decided that gene therapy would be an initial thrust for the cancer center. I guess this was also the same time I was working on Genesys Therapeutics, so I was really thinking about it a lot, and it's applications to cancer. So, we made that a high priority. And we were the first non-profit group to treat, to do some gene therapy work here clinically. But our goal, our focus is really on biological approaches to cancer, so in addition to gene therapies, antibody-based therapies, vaccine therapies, and so forth, but the research program at the institute, I can give you an annual report. It has a variety of programs including a strong molecular biology program, gene discovery, we have the gene therapy program, we have a cellular immunology program, we have a retinoid program, where Magnus Fall is discovering small molecules, retinoids, that are inhibitory to cancer. We have a guy working on apoptosis. I mean, there are really, and we have a new clinical program that is designed with Sharp, jointly, supported by Sharp Health Care, so there's a variety of research going on here, and I still have a grant with antibody-therapy.

JONES: So where did you recruit people?

ROYSTON: A lot of the people were recruited in the area, people that I could recruit within San Diego that weren't going to be too expensive.

JONES: UCSD? Scripps? Salk?

ROYSTON: Yeah, Salk, Burnham Institute, UCSD, there was an old institute called the California Institute of Biological Research, it was a non-profit affiliate of Stratagene. I recruited a scientist from there who's very good. Got a guy from Case Western Reserve that we recruited, and there are some people from out of state, but the main people are people in San Diego, where it's fertile ground.

JONES: You've been in cancer research a long time. Where do you see immunologic approaches to cancer, from the time when you started to what's happening now?

ROYSTON: This idea has been going on for so many years, you know, it goes back to the turn of the century, but if anything, there is just more and more data emerging over the years since I've been in cancer research to suggest that the body can mount an immune response against cancer. It just needs a little help. There seems to be, the

ability to mount a response is there because, and its understood, because cancer is due to a genetic alteration, and when you have genetic alteration, you have alteration in the proteins, because that's what genes make are proteins, and if you have altered proteins, they ought to be recognized as being foreign by the immune system. And it doesn't have to be a external [?} it could be a protein within the cell that is expressed in a peptide form on top of the, expressed by what we call the MHC molecule. The basic premise, without going into any details, if you have an abnormal alteration of genes, then you should have an alteration of protein, which then should be immunogenic for the host, and we've been able to show this consistently in animal models, and what we've shown is that the immune system really needs a little help in recognizing these subtle differences, and that's why the gene therapy approach of putting genes into cancer cells that secrete, that cause the secretion of what we call cytokines that stimulate the immune system become very useful. We also know that these tumor cells also make suppressive factors that inhibit the immune system, so that by blocking those we can get an immune responses, and we're trying to translate that into human applications and it's very difficult because taking patients with far advanced cancer and using these techniques, which are actually quite mild, like vaccination techniques, it's hard to show any efficacy because the patients are very sick and the tumors are growing and they're so large. So we do think that the major application of these therapies will be before patients relapse with tumors, so after the first treatment, after surgery, one could introduce these therapies and prevent the tumors from coming back. We also have shown that even when patients don't respond, we can still see evidence that we're getting immune responses to their tumors.

END INTERVIEW

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