



LIFE SCIENCES FOUNDATION

The Life Sciences Foundation Oral History Program

Robert F. Johnston

Interview conducted by Mark Jones, Ph.D.

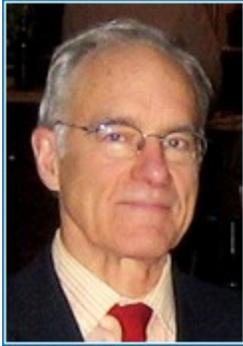
Hanover, New Hampshire 4th April 2012

Copyright © 2012 The Life Sciences Foundation

LSF is assembling a virtual oral history archive – we are recording, transcribing, and publishing interviews with leading figures in the biosciences and the biotech industry. These documents contain stories about the history of biotechnology that have not yet been heard by scholars, journalists, and the general public.

Biography of Robert Johnston

After graduating from Princeton with a degree in economics, Robert Johnston began a career in investment banking at F. S. Smithers in 1960. He moved on to Smith Barney, and then established his own investment company, Johnston Associates, in 1968. He paid attention of advances made in the life sciences during the 1970s, and recognized the implications for industrial processes in several fields. In 1977, he founded Genex, a recombinant DNA company. In 1980, he established Cytogen, a monoclonal antibody firm. Other Johnston Associates' life sciences ventures included Ecogen, Sepracor and Biocyte. The Johnstons are involved in education reform, nationally and internationally.



Robert F. Johnston 1936 ORAL HISTORY PROGRAM ROBERT F. JOHNSTON

Date: 4th April 2012

My father was an automobile distributor. He had been in that business almost all his life. He distributed Cadillacs and Mercedes Benz. He sold Pierce Arrows during the Great Depression, which in that day was like selling \$500,000 cars. The Pierce Arrow factory went bankrupt. Guess what happened to the distributor. He went bankrupt, too. You could say I grew up in an entrepreneurial atmosphere. My father was clearly an entrepreneur. His parents died when he was young. He raised himself, and a younger brother and sister.

I began working for a small investment banking firm called F.S. Smithers and subsequently went on to work for Smith Barney.

In 1967, I went into business for myself and did some merger and acquisitions. The focus then was the computer industry. I did a merger for a company called Interdata in New Jersey, one of the first companies to develop read-only memory. They got some funding from a local wealthy businessmen who believed in the concept, and I raised a million and a half for them from Bessemer Securities, which was a big deal then. I did a couple of computer software deals with a friend of mine, a member of the Phipps family.

I then moved into the medical area. I began reading articles and talking to professors at Princeton. I became intrigued with molecular biology. I was reading scientific publications and there were more articles on molecular biology than any other area. Clearly, the scientific community was interested in it.

Monsanto had already convinced and had invested in Genentech or had a contract with Genentech. Monsanto had said they would like to make some investments in the area. Jerry was receptive, and was located in New Jersey. Then, I sent letters out to many companies. Koppers responded. All of a sudden, the Vice-Chairman of Koppers, and the head of R&D and another gentleman showed up at Genex. Les and

myself, and a secretary, and maybe one other scientist were there. That was it, but they were interested and put up \$3 million.

Their interest was skipping three generations of technology. They were creosoting railroad ties. Compared to a company like Dow, they weren't even on the playing field, but they were gentlemen, and great people to work with. We did another financing with them. We did our initial public offering with First Boston, their investment banker, who also knew nothing about this area.

We had a lot of breaks that we didn't appreciate at that time. For example, Mitsui & Co. Ltd. was so intrigued with this technology that they came in and translated all of our scientific material and took it to Japan. We paid them when deals happened, and they did a couple of deals for us in Japan. We got a lot of free publicity which helped with our second public offering. The Genentech IPO helped us. Nobody had heard of Genentech, but when they came out and the stock shot up 300%, suddenly everybody knew them.

The mistake we made was that we didn't focus on the pharmaceutical business. That's what Amgen did with EPO, but they were doing other things, too. All of us at the beginning thought we could apply genetic engineering in various industries. But the issue was how long to stay with it. Most either dropped it or spun it out, as Genentech did. They created Genencor as a separate business. What we did wrong with Genex was spend too much time and effort on the chemical industry. The chemical industry has pretty narrow margins and pharmaceuticals had big margins and big PE's [price-to-earning ratios]. We had good scientists. We could have done good things in other areas.

This industry is like any other. It's full of 'what ifs?' At one point, after I became the CEO, I had three choices. The company had this big plant down in Paducah, Kentucky and we had been cut off from the contract we had with G. D. Searle, on NutraSweet.

Shapiro, the guy who was running that company, was tough as nails. Can you imagine getting your label on the Pepsi-Cola can? That's what he succeeded in doing – that was a real feat. We didn't have a long-term contract, but we had bought this plant. We were only using about 10% of it, so when the contract got terminated, we had big problems. I had a choice between three different groups. One was the bankruptcy lawyers, another was a venture group that was interested, and the third was George Rathmann of Amgen. Obviously, with 20/20 hindsight, we should have sold the company and merged it with Amgen. They were nothing then. They were still struggling.

Cytogen was a monoclonal antibody company. I found Tom McKearn at the University of Pennsylvania, who had just written a book on monoclonal antibodies. He was knowledgeable in the area. Another person you could talk to who has been in the game a long time was Steve Chubb, Cytogen's first CEO. Steve is part of what they call the 'Baxter Mafia' in Boston.

The basic strategy was to use monoclonal antibodies. Tom developed methods to link antibodies covalently to solid surfaces for diagnostics tests for sexually transmitted diseases and blood separation processes; to radioisotopes for imaging and therapy; and to chemotherapies for cancer treatment. Tom came up with the technology, and we had the first patents for attaching radioisotopes to the constant region of the antibody. The antibodies were delivery vehicles for radioisotopes. We used certain less lethal radioisotopes for imaging purposes. We injected the antibodies, which targeted the tumor, and we got radiographic images of the tumor. Then, you could attach a more lethal isotope, and you could kill the tumor. So we raised money. We had these pictures of mice; we injected tumor cells and they developed big lumps. Then, we injected them with antibody and radioisotopes, and that would shrink the tumors.

We put these pictures in a prospectus. The SEC thought they were too promotional. They didn't like that, and made us take the photographs out. As it turns out, it was not the best science. It was too early. Ron Cape once said to me, 'If mice could pay, we would all be in great shape.' But the reality was that since the tumor was injected, it wasn't a tumor that grew naturally. It turned out that the therapy wasn't quite as efficacious in human beings.

The initial money for Cytogen came mostly from Boston—it was Ampersand and Narragansett Capital in Providence, which Royal Little started after he retired from Textron. Bob Stockman was representing them. It was Ampersand, Narragansett, and Charles River, which was more into biotech then.

It was easier to raise the money. By then, everyone thought I was a genius. I raised the money for the business plan and to get Steve Chubb and Tom McKearn in place. Tom was a recognized scientist in monoclonal antibodies. Steve had been running the diagnostic side of Hyland, Baxter's subsidiary. Baxter had guys in biotechnology. There were about five or six people up in Boston that came out of Baxter. Henri Termeer, Carpenter, Schmergel, Ted Greene in San Diego, and there were others.

I put up the seed money to start Cytogen, and then we got money from American Cyanamid. Their CEO, George Sella, felt intuitively that this area was going to be significant.

We had the money from Cyanamid but we were running through that. Steve Chubb and Tom McKearn didn't get along too well. So Steve left, and I got Ron Brenner, who was near the top of R&D at J&J. Ron was a delightful guy. I didn't do enough diligence on Ron. When he was at J&J, he was great at spending money, but we didn't have too much money, so we couldn't afford to spend too much, and we almost went under. We were on a family trip in Inverness, Scotland, and I got a phone call from the CFO who told me we couldn't meet payroll in three weeks. The guys at Charles River had said they would put up the money, but they wanted an option on half of my shares at my cost. I owned about 30% of the company. I said 'that's an expensive deal.' We had planned to do a public offering for about twelve dollars a share, the cost of my shares was fifteen cents. I remember walking on the beach at Inverness with my wife, and saying, 'I didn't sleep last night. I don't think I'm going to sleep tonight. I think we should go back home and address this problem.'

I went to see the bank. I got a second mortgage on the house and I said, 'OK, I'll put up my share, three hundred thousand dollars, and everybody puts up their share.'

In all fairness to Ron Brenner, he did a lot to help us recover. He was schmoozing Thomas at Kodak, who was head of R&D. Kodak wanted to be in the pharmaceutical business, so we cut a deal with them. They got the rights to the monoclonal antibody therapy for killing tumors. I think it was twenty-five or thirty million dollars and it made a big difference. Then we did the public offering with Donaldson, Lufkin & Jenrette. Our banker was Tony James, who is now the President of Blackstone. About three or four days before the offering was going to be effective, Tony called me up and said, 'Bob, if you want to sell some shares, you can sell three hundred thousand shares because this offering is way over subscribed.' We would have had to delay the offering by two or three weeks, rewrite the prospectuses and distribute them, and there has to be a certain time period to do this. I told him I didn't think the delay was a good idea. So I didn't sell any and we did the offering. It didn't see that price for another two years! If I had delayed it, there wouldn't have been any offering or it would have been for a lower price, in that two-year time period, I could have used the money. In any event, this is an example of a company that basically couldn't meet the payroll in about three weeks and then, all of a sudden, had \$60 million in the bank.

In 1987, the market went down 500 points in one day. 500 points as a percentage was a much bigger deal

then that it is today. I had a meeting with Ron about a week later. Ron said, 'We need to raise another twenty-five or thirty million.' I said, 'Ron, the world is different than it was before. I can't do it.' He said, 'We got a deal here, I run the company, you raise the money.' I said, 'Ron, we have to cut overhead. I can't get any more money for a while, this isn't J&J.' He wasn't very good at cutting overhead.

I was always particularly intrigued with desalination because it is a big need and a big problem, and that was the basis for starting Sepracor. Jack Quinn, at the University of Pennsylvania and was knowledgeable about separations, and Tim Barberich, a businessman with a background in separations, who had left Millipore and was trying to start a company of his own. He had a scientist at Columbia University who was difficult to get along with and kind of controversial, but a pretty good scientist. We talked to Tony Evnin at Venrock, and to Chuck Newhall of N.E.A. I was trying to solicit competitive bids, and each of them were interested. Then I got this telephone call from Jim Blair of Rothchilds. He said, 'Bob, we're prepared to make you an offer and it's the three of us who're going to make the offer together.'

Sepracor had technology that could separate optical isomers. In many drugs, there are two components that are mirror images of each other so it's not easy to do the separation. The company had to decide if it was going to be a service business for the pharmaceutical companies. Les Misrock, a litigating patent attorney at Pennie and Edmonds was terrific at this early stage in the biotech industry. He built up a practice with lawyers that he sent to learn about biology.

Les was very creative, very imaginative. He had a mind like a machine gun. I give Les a lot of credit. He became the patent attorney for every one of my companies after Genex. Genex had its own lawyer down in Washington. Les was pretty aggressive so he was a little controversial among lawyers. As well as being the lawyer for Cytogen, he also found one or two of the key products. Unfortunately, Les had prostate cancer. If you get prostate cancer early in life and it's aggressive, you die from it. If you get prostate cancer when you're over 65, it's much slower. Les had the aggressive kind. I remember meetings with him late in his life when he used to take five pills every hour. He took me to a benefit Cap Cure put on by Michael Milken. Milken got up and identified Les as the longest living survivor. Les knew all the other prostate cancer guys. One of Cytogen's key drugs was something Les found because he'd spent time at every major cancer research center – Roswell Park, Columbia, MD Anderson, Sloan-Kettering.

That's much more value-added than being a service business, for sure. It's expensive to write all those patents. At first, we went to these companies and said, 'We have data on four rats and three rabbits,' and they just stared at us. We raised more money and developed our data. After our initial meetings with, Eli Lilly, the CEO of the company brought in his head of R&D and his head of patents and asked them, 'How can this little scrawny company over here basically have patents on our drugs.' They did a big deal with Sepracor.

We ended up doing a deal with Lilly on the R-Fluoxetine, which is the R-form of Prozac. The ideal would be to end up with two drugs with different functions. Normally you end up with one that is clearly a good drug and one that isn't or is a problem. The complication is they saw Prozac coming off-patent, so they spent \$200 million on clinical trials. The problem was that they pushed the dosage of R-Fluoxetine up about 500% from what it was in Prozac and they got a slight QT (heart rhythm) side effect. The FDA had become much more sensitive about QT side effects and Lilly knew they would not get FDA approval.. I question whether they had to go that high. The answer is probably not, because you still could have had a differential effect. When Prozac went off the patent, revenues dropped precipitously. So that was one of the things that went wrong in 2000 and 2001, when Sepracor's stock went from \$140 to a little under \$10. It probably never should have been that high. All these stocks were out in outer space at the time, in late 1999, early 2000. Several other failures also contributed to the demise. They'd had an extensive pipeline,

but they had to cut back, and had to focus.

Tim did a great job for the company, he was a great salesman. There haven't been too many CEOs that have lasted for a 25-year period. Henri Termeer was one of the few others. Sepracor then came out with a drug for sleep, Lunesta. They said 'we're going to sell it ourselves.' They already had a drug, they were selling themselves. They had raised the price and were selling it at 10 times the generic price, and were doing well. So they thought they could do this but the problem is that you've got to sell a sleep drug to general practitioners. So you have to have more than 2000 salespeople plus you have to do the direct consumer advertising. So suddenly you're spending \$150 million a year or more on DTC, direct-to-consumer marketing.

In a partnership, the partner would be spending all that money. The drug had a very successful launch. It went up to about \$700 or \$800 million a year and then it leveled off. Then Ambien came off patent so that became a lot less expensive. Ambien had long term release which was easier to sell. They had these ads explaining that the coating releases slowly. The problem before was Ambien had only lasted four hours and people want to sleep for seven hours.

Then we created another company, i-Stat. i-Stat was more on the device side. It was a handheld blood analyzer about the size of two cigarette packs. You could take a blood sample for 'bedside and patient point of care' diagnostic testing. The most obvious application was to have it used in ambulances so that some of those results were obtained before they got to the hospital. Also because it needed only a little bit of blood it could be used on neonates if you wanted to get a fast, accurate reading.

The key funding came through Jack Whitehead. Jack had sold Technicon at that point. He became one of the first billionaires in the field when he took Technicon public in 1972. He was worth well over a billion dollars. I approached him regarding I-Stat with a certain amount of trepidation because he had looked at financing technology out of Salt Lake City that was the same area as i-Stat.

Jack was very open to new ideas and joined the board. That was the time when Jack got involved in other venture deals, though he was not a particularly good venture capitalist because he was used to doing things his way. Needless to say, that is not the normal role played by a typical venture capitalist. So he actually got out of some of the deals when he didn't agree with management's ideas. i-Stat, however, was right in his sweet spot of interests. He never fully understood the technology. Compared to the Technicon instruments that used fluid based analysis, i-Stat was semi-conductor based, which meant you had to get the volume up to get the manufacturing cost down. It took much longer to get the volume up than we had planned.

We made Jack chairman of the board because he kept putting up more money, and from my point of view, he and I were the major investors. I started out as the major investor but eventually he became the bigger one and it was like playing poker with an 800-pound gorilla. For example, Jack would say, 'I think we want to do two more diagnostic tests. I'll put up my million bucks, and you're going to put up yours,' but I didn't have that kind of money. His response would be: 'Well, I'll put up mine, but I'm getting such and such percentage for it.'

Jack had a place in Aspen. We'd drive up to Westchester County, get on his plane and fly out to Aspen. We'd have a board meeting Saturday morning and then go skiing. The rest of the board meeting would be after dinner. After you'd had a nice dinner, and a nice red wine, Jack would say, 'OK, I want to review where these stock options are going, and I want to review where we're spending our money.' Everyone else is half asleep by this point. They've had a tough day skiing, they're exhausted, and they've had a nice

dinner. Jack got a lot more of what he wanted by doing it that way!

One of my white hat ventures, Envirogen, dealt with microbial degradation of toxic waste materials. The initial area we looked at was PCBs which have not had much publicity recently but every one of the natural gas transmission companies had big liabilities on their balance sheets for PCB activities. Their pumping stations used the PCBs to keep them cooler. They pump the gas through and when the PCBs are exhausted, they are expelled.

The biggest one that got publicity was General Electric for its coolant. GE had a plant on the Hudson for which they incurred big fines. The problem with cleaning it up was that if you start to dig it out of the soil it's going to affect downstream. So GE agreed to spend money on biodegradation, microbes that would deactivate all the PCB's. The cleanup costs were a couple of hundred million so long term it was a smart deal for them to invest in researching alternatives. It also looked like there was a market for it. The federal government passed laws mandating cleanups. We thought we would get into that business—biodegradation of toxic waste materials. The problem was the federal government never put any teeth into these laws.

Allen & Company was the major outside investor in Envirogen and then they took it public. Ron Untermann who had been at GE working on PCBs was head of R&D. It was a good team but it was always a struggle, and we worked on MTBE. It was an additive in gasoline and it was mandated in California and the problem was it was toxic. Nobody ever proved it was really due to MTBE. It did affect your thyroid. It was in the water, you could smell it if you were taking a shower so you knew you were being exposed to it and there was good medical evidence too. They were even trucking water in to Santa Barbara and a couple of places where there had been leaks at gasoline stations.

We finally sold Envirogen to Shaw Environmental. Ironically, some of the contracts we were working on for years finally came through for them. They are happy with it.

The problem is all the ones that aren't great successes you spend a lot more time on.

Biocyte exemplifies a characteristic of mine – being too early. Hence my favorite saying: the pioneer is the guy with the arrows in his back – because he gets out in front of the wagon train.

Biocyte approached me through Lewis Thomas, one of the directors I brought into Cytogen. He wrote 'The Lives of a Cell' and used to write a column in the New England Journal of Medicine that he put together as a book. He's written four or five books. He's a Princeton graduate who was head of Sloan-Kettering and he won the Madison award some twenty five years ago, at Princeton. I approached him after his acceptance speech, asking to meet with him. He looked at Cytogen's work on monoclonal antibodies to kill tumors, which was cutting edge research at that time, and was impressed. He was a director till he got ill and had to leave the board. I remember what he said about one of our products: 'This product is doomed to succeed.' He loved the play of words- you can see that if you read 'The Lives of a Cell'.

Lewis was a founder of Biocyte their plan was to collect cord blood stem cells and use them therapeutically. This was twenty-five years ago, in the mid-1980s and it was an idea way ahead of its time. Well before George Bush made stem cells famous by banning them -which was just stupid. The people initially interested in this were those with a disease called Franconia's anemia. If you had it, you died by the time you were eleven or twelve years old. We paid for a study at the Saint-Louis Hospital in Paris. People whose child had the disease would have their second child tested at birth. If they didn't have the genetic defect for Franconia's they would collect the cord blood stem cells at the time of birth. Then the

first child would go through radiation where the immune system was wiped out and then it would be reconstituted with stem cells from the second child. Generally, the odds were good that the immunological profile of the second child was close to the first child's profile and so there would be less risk of rejection. After a couple of these operations, the data revealed that the kids were living for a year or two more. I don't think it turned out to be very long term. We then set up an operation at Magee-Women's Hospital at Pittsburg to do this on a bigger scale. It wasn't cheap but people are still doing it today.

We never promoted this research. At Magee Women's Hospital, the people at the lower levels were really excited. They wanted to do it, but the administrative level hadn't quite bought into the concept and so they wouldn't let us solicit pregnant mothers ahead of time and explain the advantages of storing your cord blood stem cells. Most of the people who were going to do it were from families where there was a history of cancer or a terminal disease within the first 30 years of life. One investor in that company was Rod Rockefeller he stored for a couple of his grandchildren. We were way ahead of the times then. Another investor was the US Steel pension fund but the manager in charge of that was having difficulty justifying it to his boss, as it was just so insignificant compared to the size of their stock portfolio.

We also started Immunicon that dealt with magnetic particles. Paul Liberti, who was a professor at Jefferson University, Philadelphia, was doing research on magnetic particles and wanted to use them in early cancer detection.

They used antibodies and magnetic particles to detect the presence of epithelial cells that break off very early in a cancer growth. You could diagnose the cancer before it could be detected with the normal methodologies such as a scan or examination. They got the money, the manufacturing, the scale-up and venture investors in place—and they took it public. They had money from Johnson & Johnson and had a marketing venture with them. We had a good investor group but the escalation and the rate of sales was way below expectations. We still had our manufacturing overheads to meet. I went off the board after it went public and the venture management did a financing using a convertible debenture because they were running out of money. Then they made a mistake by deciding to sue J&J, blaming their lack of investment in the marketing for the poor sales. They lost the suit and J&J bought the whole thing for \$25 million which was the value of the convertible debentures. So the debt interests walked away with their money and the common shareholders got nothing. think it is doing okay. There is a need for something like that in the market.

There was another company we were too early with too, called Seq. This was Kevin Ulmers' dream—from Genex. The challenge was how to detect the ATCs and Gs separately, there were all kinds of ideas about how to tag them. Kevin's novel idea was that if you dropped the temperature, enough A, T, Cs, and Gs would fluoresce, which meant you didn't have to tag them. He was the first guy to believe you would be able to sequence a genome for under \$1,000 before everybody else did. Another guy working for me, Richard Horan, fell in love with this concept and convinced me that we should take it on.

It was a good idea but three or four of the technologies were unproven. The odds of success were only about 20%. We got some money from Bristol Myers and did research there. We had Arnie Levine, head of the molecular biology department of Princeton University who subsequently moved to running Rockefeller and is now at the Institute for Advanced Study. Arnie is also the guy responsible for the p53 gene. Arnie is really smart, understands molecular biology really well, and his intuitive instincts for what works is also pretty good. He felt it wasn't going to work. So we repositioned the company to detect movements and intracellular pathways and finally sold it to Amersham, who in turn, sold it to GE. I think it's working but for us, it was a long tough slog, and we never got the sequencing bit quite worked out.

Now, I'm trying to partner with some pharmaceutical guys with my company, Zywie LLC. I think we're going to finally end up being able to do that mainly because there's some interesting data coming out of Japan. The drug we have for Gaucher disease is Ambroxol, a mucolytic agent that's been around for about twenty years but never brought in to the US but very safe. So it looks like there's going to be some data generated that proves it goes across the blood-brain barrier and is efficacious in treating Type III Gaucher, for which there is no drug right now They have to go across the blood-brain barrier to treat it and Cerazyme does not cross the blood-brain barrier.

Maybe, another key part of this story is that playing this game becomes an addiction.

People ask me what you need to be a good venture capitalist and I say you should be a psychiatrist. Because the key thing in the game is to pick the right president, the right CEO, and pick a guy that can build a team, who can understand the science, can sell it and so forth.

Recommended citation:

Robert F. Johnston. 2012. *Independent Biotech Venturer*. Oral history conducted by Mark Jones. The Life Sciences Foundation, San Francisco, CA.

The Life Sciences Foundation, One Embarcadero Center, 27th Floor, San Francisco, CA, 94111