Doug Jolly

Interview conducted by

Mark Jones, PhD

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Doug Jolly

Dr. Douglas J. Jolly, Doug, Ph.D., is Co-founder of Tocagen, Inc. and serves as its Executive Vice President of Research and Pharmaceutical Development. Dr. Jolly served as the President and Chief Operating Officer of Advantagene, Inc. Dr. Jolly is responsible for numerous clinical trials. He served as Vice President for Scientific Affairs of Chiron Corporation's Center for Gene Therapy. He has advised the US National Institutes of Health and the FDA on scientific strategy and regulatory issues. He has an extensive experience in moving new vector technologies through the regulatory processes required by federal agencies including the FDA and National Institutes of Health (NIH). Dr. Jolly served as the Chief Executive Officer-BIOMEDICA Inc. of Oxford BioMedica PLC. He co-founded Viagene Inc. and served as its Vice President of Research. He is an internationally recognized expert in the field of gene therapy and its industrial application. For most of the last twenty years, Dr. Jolly is a senior biotechnology executive, involved in translating gene-based products from research through clinical development at the following companies: Viagene, Inc., Chiron Corporation, Oxford BioMedica, Inc., and Advantagene, Inc. He served as a Director of Oxford BioMedica PLC. from May 2001 to March 2, 2004. He is a leading figure in gene technology in the USA. He has published over 100 scientific articles. He is an Inventor on over 45 US and European issued patents. He is highly respected as a pioneer in the clinical application and commercialization processes for gene therapy product candidates. He serves as Chairman of the Industrial Liaison Committee of the American Society of Gene Therapy (ASGT). Dr. Jolly pursued his academic career in Biophysics and Molecular Biology at the Weizmann Institute, Harvard Medical School, Scripps Clinic, the University of California, San Diego and The French National Institute for Health and Medical Research (INSERM) in Paris, France. Dr. Jolly received his education in Scotland, and holds a PhD in Biochemistry from the University of Glasgow.

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THE SAN DIEGO TECHNOLOGY ARCHIVE

INTERVIEWEE: **Doug Jolly**

INTERVIEWER: **Mark Jones, PhD**

DATE: **June 25, 1997**

LOCATION: **San Diego, California**

JONES: OK, David Hale's first day at Gensia?

JOLLY: So, Harry and Paul had been hawking Gensia around San Diego for, I don't know, for a year or so, and they got Hale interested, and the timing was right because he sold Hybritech. And so, they had an office, I think it was on Flintkote Street, up here, where Paul Laikind used to come and sit. So, David had been to see him a couple of times, and the day that he started, they moved, and so David was really diving around Sorrento Valley looking for Gensia, 'Where's this company I just signed up with?'

JONES: Well, let me ask you about your early career. You have undergraduate and graduate degrees from Glasgow in biochemistry?

JOLLY: Right.

JONES: Why did you decide to go into biochemistry?

JOLLY: Biochemistry? Well, I did a PhD because I couldn't think of anything else to do, and I got interested in biochemistry, I was undergraduate in biology, basically, and so, what fit my interests best at the time was biochemistry. Since that was really the major biological science to which I was exposed as an undergraduate.

JONES: And then, when you did your graduate work, did you have in mind a typical academic career path at that point?

JOLLY: Well, no. Actually, you know, I decided to see the world as a post-doc, not quite that consciously, but I certainly wanted to leave Glasgow. I'd lived there all my life, and although it's not as unusual as it is in the United States for people in Glasgow

to stay and do their undergraduate and graduate degrees in one place, I'd had enough of the place. Although, actually, I love it now. I've been away long enough. So, I was looking for somewhere to go, and I actually looked for post-docs, and the two places I almost ended up, one was Berkeley, with a guy named, you can tell this is the place I didn't go, what was the guy's name? Wong, Paul Wong? I've forgotten his name. Anyway, he's still around. The other place was the Weizmann Institute in Israel, and the Weizmann Institute had the money, so I went there, which was a great experience, actually. Very interesting. And then, after two years there, I had to find another job, so I still wanted to come to the States and see what it was like, and I got a job as a post-doc with Charlie Thomas at Harvard Medical School. I got there about 1975, and it was kind of like getting a PhD all over again because molecular biology, the current era of molecular biology was just starting, restriction enzymes had just been found, cloning was just happening, so I learned, basically, how to be a molecular biologist there, and when Charlie moved from Harvard Medical School to Scripps Clinic, he got invited to Scripps clinic to start, as he said, a cellular biology department. So, people said, 'Do you mean cell biology?' And he'd say, 'No, cellular is an adjective.' Anyway, Charlie tried to attract a number of people like Zuma Tonagawa and Dick Flavelle. Tonoagowa has a Nobel Prize now, and he didn't he get quite the top level of people that he wanted, so after about a year or two he had a big fight with, who was the guy who was head of Scripps Clinic before Lerner? Anyway, he left and found, I left Charlie before then, to go to work for Ted Friedmann at UCSD in 1980, but Charlie left, and this is kind of interesting, to start a research institute called Helicon, and also Syntro, which is a barely extant biotech here in San Diego now, and so, and Charlie is kind of an abrasive personality in a lot of ways, and after about a year or so, the staff rebelled and told the Director of Syntro, that they were all leaving, or Charlie had to, so they gave Charlie Helicon, which still exists down in PB. It's kind of a low class incubator for biotech companies, and actually DepoTech started there, I think, yeah.

JONES: People who were there started Depotech?

JOLLY: The people at Depotech used Charlie's Helicon Institute, which is three nissen huts, down in PB, which also has an interesting history, which I'll tell you, since we're doing history. If you drive down 5, there's a whole set of nissen huts, on a thing called Santa Fe Drive. I guess they're on the left side of the freeway going south, and Santa Fe Drive actually starts on one side of 5, and runs underneath it. And some of those are now, I don't know what the original purpose was, but some of those are

antique stories and things like that. But at least three of those were built by this guy named Grant Bartlett, who was the, probably, first guy to figure out that if you had an NIH grant, you could start your own institute. So probably in the late fifties, let's see, is that right? Yeah, the fifties, he started his own institute there, and managed to buy the three nissen huts with his NIH grant, and like twenty-three years later, he finally didn't get his grant renewed, but by that time, he'd bought the land. I don't think you can do that with an NIH grant anymore, but he rented them out. That's how he made a living, he kept one for himself, and rented the others out. So he rented one out to Charlie, so that was where Depotech started. Anyway, sorry, so I went to Ted Friedmann's lab, I took my molecular biology tools there from Charlie's lab, and they didn't really have any. His was a polynoma and virology lab at the time, and you know, Ted had always been interested in gene therapy, and next door was Jay Seegmiller, and that's where Harry Gruber and Paul had met, actually I didn't know them, although I was there before them. And I cloned a human HPRT gene there, and that corresponded to genetic disease, and so that kind of fit together, and we started trying to do gene therapy. And the initials attempts, we were using calcium phosphate transfection, and that wasn't working very well, and I went to a conference in 1982, called 'Tumor Viruses and Differentiation,' that's a keystone conference, which is one of these ski conferences. Everyone goes for a week to a ski resort and you supposedly do the academic stuff in the mornings and the evenings, and you go skiing in the afternoon. And it's actually very good, because you can track down someone and jump on the same ski lift with them. They can't get away from you. Anyway, at this meeting, this guy named Richard Mulligan, who's now professor at Harvard, Mass General, yeah, found the retroviral vectors, so I went back to see Ted and I said, 'Oh, retroviral vectors are the way to go, ' and we'd already started collaborating with Inder Vermer, at Salk Institute, because I thought I was never going to clone an HPRT gene to do something, some stuff with retroviral vector bits and pieces, so we started trying to make retroviral vectors with Inder, and Inder was just getting out of the stage where he actually worked the lab, and he was putting together bits and pieces in the lab, and giving them to me, and they turned out to be more or less junk, because he didn't quite know how to do things right. And so then he a post-doc called Dusty Miller coming, who's now up at Fred Hutchinson in Seattle, and he's now a big wheel in gene therapy, so Dusty got to make the vectors and put the HPRT gene in, so that started the retroviral vectors. Once we had them kind of up and running, Harry was always interested in gene transfer, and he had started growing human marrow cultures, in Jay Seegmiller's lab, so we collaborated

on a paper that we published in Science, in 1985, about putting genes into whole mouse cells. So, that bit is the connection where Viagene met Gensia. Because, at the same time, Harry felt that he had a couple of purine compounds that looked kind of interesting.

JONES: They called it Retrogenes in the beginning? Were you aware of it when they started it?

JOLLY: Yeah, what happened was, I stayed at Ted's lab for actually just about six years, a long time. So the postdoc there, was one of those glorified postdocs, what do they call them? Assistant research biochemist, or assistant research scientist, something like that, where you can get your own grants, but you are behoven to someone for space. And I was finally realizing that this was not the right career path, well, that it wasn't, you know, that I couldn't be there, so I actually got a job in France with a guy named Etiene Emile Gaulieu. I worked for, so I actually became a French conseiller, because he got me jobs. And he's famous for two things, well he's famous for other things, he's a steroid biochemist, but he's most famous for two things, one is he's actually closely associated with RU-486, and in fact, there is some edition of the New York Times Sunday Magazine with his full page picture, Mr. RU-486. And the other thing that's he's famous for is being Sophia Loren's boyfriend, so guess which one he's most famous for, right?

JONES: And he was at INSERM?

JOLLY: Has he just retired? Yeah, he was at INSERM in a place called Clairnan D'estet, which is just south of Paris, about a hundred yards south of Paris. He had a, I forget exactly how I met him, but he used to come to the Salk all the time, because Roget Guillemin was in the basement, and he's the guy who eventually moved to the Whittier Institute. He's a Nobel Prize winner in peptide hormones. So, I met him and we kind of hit it off, and so he said, 'Well, you can come,' this is one the patron types deal, 'You can come, I'll get you a job. You do whatever you want, but I just want someone around who knows how to do molecular biology.' So, I said, 'OK.' I also wanted to go back to Europe and see what it was like, so, but before I left, I'll always remember, Harry came up to me, I was going to leave, I'd taken the job, I'd said, 'OK, fine, I'll do it.' And that was about July, I think, and I was going to leave about the end of September, and Harry came up to me in July, and said, 'You know, I think I've found a way to do research without writing grants.' So, I said, 'Oh.' He said, 'Yeah, I

talked to this guy and he said we should form a company, and you know, I have some stuff, but also this gene therapy is kind of interesting. Why don't we form a gene therapy company?' I said, 'You know, that sounds like a really interesting idea, and I'd be very interested in doing that, but I just took a job in Paris.' And he said, 'Oh.' So, we talked about it a little bit, and I said, 'Well, you know, I'm going to go to Paris because it looks like an opportunity, How about, we should keep in touch?' Actually, what that meant was Paul and Harry got to do the legwork, and I got to be in Paris. And so they started Gensia with the Viagene technology, with the Retrogenes technology in there, in '86. And I came back several times, and eventually, they wanted me to come back and run the research for Viagene, for Retrogenes, that was spun out. And actually I hesitated for a couple of months. In fact, I turned them down at first, and then I called them back and said, 'No, no.'

JONES: Did you perceive a risk? This was a lifetime position, right?

JOLLY: Yeah, that's right. There was that. Basically, that was part of it, I was in a life, I mean living in Paris is a lot of fun, but scientifically, I was kind of, I'm not sure I was really getting anywhere. And also, you know, I was really interested in gene therapy, and I really wanted to make it work, and when I sat down and thought about it, the only place that you could do that was a biotech company. You just couldn't get the resources in academics. And I now know that large pharmaceutical companies never really set aside enough money to do anything like a biotech company does. I didn't know, of course, all of the things I know now, but I kind of had that understanding, and also, basically, I said, 'If you don't do this, you're going to kick yourself for the rest of your life.' So, we negotiated some more and I came. So, yeah, I resigned from my job for life, yeah.

JONES: When you did come back, they hadn't spun off Viagene yet, it was still part of Gensia?

JOLLY: No, it had been separated. I guess it was incorporated in February of '87, and there actually was a place to sit within Gensia. I guess the first employees, I forget the middle part, I know Brad was number one, Brad Gordon was number one.

JONES: In management, of Viagene?

JOLLY: Yeah. Then there was a scientist and two technicians, one of whom is still here, actually. And a secretary, that's right. So I was employee number five. And there

was nothing really, I mean, it was an empty space. So my job was to hire a bunch of people to start the company, essentially.

JONES: And how did you go about doing that, who did you recruit?

JOLLY: Well, I did it basically by networking, I was in science so, I got two guys from Inder's lab, Inder Verma's lab. One was a guy named Dan St. Louis, who lasted about, probably had too explosive a personality, let's put it that way, to work in a company, and the other guy was Jack Barber, who actually stayed here for quite a while, and now he's, I forget what his title is, but he's part of Immusol, which is Flossie's company. So I hired basically four scientists in the first year, year and half, who led bits of Viagene for the first three or four years at least. So, Dan left, so there was Jack, I hired Steve Chang, who's also still here, who was actually a competitor of mine for cloning HPRTG and making retroviral vectors, so I knew him that way.

JONES: Where was he doing that?

JOLLY: He did that in Houston, with Tom Caskey, who's now head of research at Merck. Steve had left Caskey and went to the NIH, but he wanted to come back to the West Coast, his wife was from the West Coast, although he's from New York. And he went to school in Irvine. And then John Warner, actually, Harry basically found John, who was our immunologist, and who's now VP of gene therapy at Inex, which is in Vancouver, it's a gene therapy company in Vancouver, just like this one. And then, I'm rambling on here. Chuck Prussak, who's still in town, but who runs the, I hired Chuck to try and start the product development piece of retroviral vectors, which he did, actually, a very good job of. Basically, the things he put together in a refined, approved manner, is what we still use. So, he went, he got pissed off because when the next generation of management came in, he didn't see eye to eye with Kerry Coles, who was the VP of product development and manufacturing. He went and got a job with the vector production lab over at UCSD. Have you talked to him?

JONES: No, I haven't.

JOLLY: And then, let's see, there was one more. Chuck, Jack, I said John, and Steve, so for the first four years, basically, four or five years, they kind of ran the research group, the four of them heading their separate groups.

JONES: Do you recall, was it difficult to convince them to come into this little start-up?

JOLLY: It's so funny, you know, people were so naive, including myself. I mean, basically, they were all postdocs. They weren't looking for a job for life, they were looking for something interesting and exciting to do, that looked like it might be fun. And, I basically convinced them that that was the case. Actually, gene therapy is still a way to sell, even quality control, in gene therapy can be portrayed as exciting, Because it's new, if you want to think about it, you can, there are issues to be solved, and that may be true for everything, but it's easy to persuade people that it's true for gene therapy. So, actually, it wasn't tough to recruit talented people, I mean, first of all, San Diego has a lot of people here, so the only person that I recruited from outside the area was Steve Chang, and I knew him directly, of that first wave of scientists. And then, we just, I mean, it wasn't, it was hard work, but it wasn't difficult to find extremely talented people. And I didn't have a grand scheme. I knew I didn't want to hire people who were all the same, which has always remained a theme here, which is you hire people for the job, you also hire them for, because they know the stuff, and I think that's worked out well, so I guess we hired about thirty people in the first year, and got up and running.

JONES: And how did you organize research? You know, these are people coming out of academic settings, but this is commercial, not a big pharmaceutical company, but...

JOLLY: Actually, you know, that was one of things I really spent a lot of time thinking about. It's one of the things I really thought about before I came to Viagene, Retrogenes. So, what's going to be different, and why is that good or bad, that kind of stuff. And you know, I came to the conclusion that a number of, or most biotech companies, I think, are out to wring money for research out of some heaven known as venture capitalists, and we'll have a good time. I mean, I know some companies that were done that way. And I thought, 'Well, it doesn't make any sense to me because that doesn't seem like a self- sustaining proposition.' And, you know, if you're going to get a company, we should want to make products, because that's what companies do. And so, I was very clear about that, and I think that's a theme for Viagene, and I don't claim to be the only person that caused that to happen, but I think that's the mindset we had, and I think that's the mindset we conveyed to people who came here, so everyone's always, no one ever took a job here thinking, 'I'm just going to

putter around doing research.' The idea was always, 'We're doing this because we want to make gene therapy products.' I mean with different, there's a large band of belief there, but I mean, for example, I remember hiring Steve Chang, and Steve said, he just took the job because he wanted to come out to the West Coast. He was interested in gene therapy, but he also said, "This stuff's never going to work,' so, I mean, Steve says lots of things, but that was one of the things he said. I don't know how much each of the individuals in their hearts believed that it was going to work. I don't think people thought that far ahead. They wanted to, they were interested in gene therapy, they were bright and wanted to do something exciting, and we gave them the orientation that, you know, we're not putzing around doing interesting experiments, we're going to try to make some gene therapy products, whatever that takes. And that's actually, because of that way of thinking, I mean, I think that's how we were able to recruit Steve Mento, because he wouldn't have come to a research boutique. So it's sort of built on itself, and that's why we have, I think, the product development capability and the manufacturing capability that we have, which most biotech companies don't have, and most gene therapy companies don't think to have, which has, I think, well, we'll see. I like to think it's turned out to be the right way to do it. We'll see.

JONES: Well, in the beginning you started off with a million dollars, right, something like that? Gensia had fifteen, sixteen, I don't know, and Viagene got about one million. Did that seem like a lot of money?

JOLLY: No. It seemed like not a lot, but I sort of had the Gensia example in front of me, which said, you can just go and get some more money if you need to, so I just believed that you could get some more money, which we did with some hiccoughs.

JONES: Yeah, was it tough doing that, going through successive rounds? What was it like presenting the science and the technology to these people?

JOLLY: It was like hell on earth in the end, because I did so much of it, because once, there was one series we had, which was called Series D, which just wouldn't close. It went on and on and on, and the VCs got warrants because they coughed up some money to keep the company going.

JONES: Is this one that Harry put some money in?

JOLLY: Yeah, Harry put some money in in the beginning. He might have put some in on Series D, could be.

JONES: Was this the one right before the IPO?

JOLLY: No, well, there were two kind of things that went on forever in Viagene's history. One was the IPO registration, for fifteen months. The Series D was kind of a replay of that, and that was in 1991? Let's see, when did Greg Phelps get fired? Because we had a CEO called Greg Phelps from October of 1988 until June of '90, I guess. Basically, he was the fall guy because Series D wouldn't close, and it still didn't close when he left, and it must have closed later that year, in 1990, but that thing dragged on for, I don't know, for about a year, and you know, we were in, we could make the next payroll, and the one after that, that kind of situation. And actually, just got, well, first of all, most of the people were younger than they are now, of course, but they had fewer financial worries in the sense that, you know, that before building families and having children, hadn't thought about worrying about this kind of stuff. So, it kind of sorted out the men from the boys in a sense, and some people left, but most people just went, 'Oh well, if we run out of money, we're out of money, we'll go get another job.'

JONES: When the money's running out, the atmosphere is not that intense, maybe? Is everybody sort of cognizant?

JOLLY: Oh, yeah. Everybody knows. We got excited about it at first, but Series D went on for so long, then we just went, 'I don't even want to hear about it. We'll just keeping working and doing the best we can until we've got no money, and then we'll stop. We'll do something else.'

JONES: What were the problems with Series D? Kleiner Perkins is involved in this?

JOLLY: Kleiner Perkins never invested in Viagene.

JONES: Oh, Domain?

JOLLY: Domain, and BIL, because they had brought BIL with them, and Fairfield and Axcell was already in there. I have to go to my meeting.

INTERVIEWEE: **Doug Jolly**

INTERVIEWER: **Mark Jones, PhD**

INTERVIEW: **Part 2 of 2**

DATE: **August 6, 1997**

LOCATION: **San Diego, California**

JONES: Let me ask you a couple of questions, just to follow up on the last time? Was Richard Mulligan the first guy to use retroviral vectors, or just the person from whom you first heard about their use?

JOLLY: No, I knew about them before, but he was the first guy who really made me sit up and take notice. I guess the first paper on retroviral vectors was published about 1981, and I heard Mulligan in 1982.

JONES: Do you recall who it was?

JOLLY: I could find the paper, I guess either Scolnick [EM] or Temin [HM], or, I guess Bob Weinberg [RA] was involved in some of that.

JONES: When you were at INSERM, had you planned to do gene therapy work there?

JOLLY: Yeah, actually I did some work on, which is, in fact, the genesis of what we did at Viagene, which was trying to start improving packaging cell lines for retroviral vectors, and actually, the only thing I ever published out of that was an abstract, and when I came back to start Viagene, I was so just so busy I never really got around to writing it up properly.

JONES: Did you ever use any of that stuff?

JOLLY: We never used any of the material, but basically the idea that if you increase the level of protein in the packaging cell line was something we tested out there, it turned out to be true, at least in some situations, and therefore, when we came here, we concentrated on doing that with the packaging cell lines, amongst other things. Actually, the other interesting thing that happened to me, I don't know whether I mentioned this or not, when I was at INSERM, I started a collaboration to make targets for hepatitis, immunological targets for CTLs, for hepatitis patients, with a guy named Massimo Leverero, and that's interesting, both because it's a, I dimly

understood the immunology at the time, but it's a precursor to some of the things that we evolved to do in Viagene, which is the immunotherapy part of it. So, that part was just to make targets, but the immunotherapy part was to use it to stimulate immune response. I'm not sure if you followed that, but anyway, he worked for a guy named Michel Perricaudet, and Perricaudet is one of the guys who basically made adenoviral vectors work, and in fact, all his stuff is now, he's had an alliance with RPR Gencell [Rhône-Poulenc Rohrer, Inc.] and I think they support his lab, they bought all his patents. So, I knew all about adenoviral vectors, right from the beginning. And we almost, I always trying to start work on them, but eventually, we decided that they had too many immunological problems.

JONES: Such as?

JOLLY: Well, they make a lot of proteins, so because we had a focus in immunology, we understood that the there were going to be issues with inflammatory reaction and elimination of the adenoviral vectors. You know, if we'd had the resources, I'd have probably started doing that, but we didn't, and so, yeah, it's kind of interesting because we just didn't take that path. We could have, because I knew about adenoviral vectors long before most people, their potential, because they'd done animal experiments before most people in the United States were thinking seriously about using them. There were some people here who were thinking about using them, but not a lot. And they first became kind of popular about 1991, or so.

JONES: Some people had success?

JOLLY: Well, they're a big piece of gene therapy now. Have people had success? Well, they're being used without thinking through the consequences of the immunological properties of them, I think.

JONES: So now they're running into problems?

JOLLY: Well, there are two issues. Adenoviral vectors, people really move fast, trying to get them to clinic, and the chief thing that happened was they were used for cystic fibrosis. And it's actually, in my opinion, a clear example of people not really thinking problems through very well, because you know, the adenovirus is a virus that affects the respiratory tract, but first of all, and the experiments I'm thinking of used Perricaudet's system but Ron Crystal who sort of drove it, but they used the adenoviral vectors just as they were, which make a lot of extra protein, and one of the

problems with cystic fibrosis is inflammation of the lungs, and so also, the preparations weren't terribly clean, and so they, in fact, at some doses in the initial experiments, saw inflammatory responses, and to this day, I don't that it's clear whether it was contaminants or the vectors themselves, but the final thing is that it's pretty clear that adenoviral vectors, although they're viruses that infect the respiratory tract, don't normally efficiently infect the cells that you need to get the cystic fibrosis gene into. I mean, in hindsight it's 20/20, but a somewhat wrong-headed approach that illustrates that molecular biologists need to know things other than molecular biology, not that Crystal doesn't, I mean, he's an MD. So, that's what's been wrong with a lot of, one of the problems with gene therapy in general is that it's being driven by, a lot of the initial technology has been driven by molecular biologists because they were doing the hands-on work, but if you wanted to take it all the way through to the end, you had to pay attention to a lot of other things, which has dawned on all of us, but some people were more surprised than others.

JONES: But from the beginning, you had the immunologists at Viagene?

JOLLY: Right, because, well the other thing, we tried to be as realistic as we could and understand that gene therapy had lots of potential, but what could it do now? And to look for ways to use gene therapy and develop the technology, but at the same time, have a potential therapeutic product, taking into account all the limitations of the technology, which wasn't very efficient, you didn't get high levels of expression, you couldn't hit large numbers of cells. Really all you could do was make protein inside some cells, and so therefore, you have to use a lever to have a therapeutic effect, and the lever most people have actually chosen to use is the immune system in one way or another, and we chose to directly use the immune system and they'd just evolve an understanding of how cytotoxic T-cell responses really were elicited, and people knew how to make antibodies more or less on command, as it were, but there was a lot of, well people weren't clear how to elicit, and still aren't terribly, how to elicit good strong cytotoxic T-cell responses. Cytotoxic T-cell responses are a major component in, you know, resistance or recovery from chronic viral diseases and cancer, so just as a sort of way of approaching those kinds of diseases, increasing the T-cell response appropriately seemed like a good idea, and one of the things that we had was the understanding that you could probably do that using gene transfer systems as they were, inefficient though they were, because you only need to put the gene into some cells, and it probably didn't matter which ones, although it probably does to some extent as it turns out, but that was the thought, and not a large number

of them, and basically what you're doing is fooling some cells into thinking that they're infected, and then doing the antigen presentation properly because there's a system for sampling the inside of cells and presenting antigens on the surface to the T- cells that are running past, and they're going, 'I've seen this one before, I've seen this one, but I haven't seen this one,' and then you get the amplification of the T-cells which starts an immunological response. So, you could take advantage of all that with gene therapy. Actually, we were doing retroviral vectors, but we're now being chased by people who want to do DNA, because it works with DNA as well.

JONES: For instance, Vical?

JOLLY: Yeah, they're doing all that, yeah.

JONES: And you're keeping close tabs on that?

JOLLY: Vical is interesting because I don't know quite what happened. We had a meeting with them in about 1990, because the venture capitalists were always going to merge us with this or the other company.

JONES: Are there common investors?

JOLLY: I don't believe so. I'm not 100% sure, but none of the major investors are in both. And actually, that was a really funny meeting. But they had basically formed, well actually Vical, I don't know how much you've talked to those guys, but originally it was formed, it was a company that was formed around lipids, and the original idea was to prolong the half-life of things like AZT, and then Doug Richman was involved in all that stuff, and somehow, Jon Wolff, who was actually in Ted Freidman's lab at the time, got hooked up with, I guess Carson, and I guess, I don't know who it was at Vical…

JONES: Phil Felgner.

JOLLY: Felgner, yeah, and they did those direct injection experiments, and you probably know the story better than I do, but you know, the direct DNA injection was a control, and the lipids didn't work at all, that kind of stuff. And that happened, I guess, about '89, and so they formed a company around it, and I know that when we met them, they had at least some data on immunological use for the DNA, but I think we showed them our data, we'd been doing it two years longer with retroviral vectors and we just told them how to do it. I mean, we must have saved them at least a year's

worth of time, I would guess. And of course, the merger never went through, so if we'd been smart enough we'd have included DNA in the patent, but we weren't, so.

JONES: Is there a lot of that kind of communication?

JOLLY: There's one other case where I can think of where we actually told people what to do, and that's with Targeted Genetics, which is an AAV [adeno-associated viral vectors], company up in Seattle, which is actually in big trouble right now, because they're running out of money, but we met with them in 1992 and, again, the idea was like 'Can we do something together?' And AAV is a field that's been plagued by 'can you make it' type issues, can you make the vector, and we went through the product development we had gotten to at that point, which was to scale up the purification and the formulation, and the effort we put into that, and I guess in our minds, to their credit, they went and tried to do the same thing for AAV, and they've actually been relatively successful, they've got a system now that makes it, which is kind of ironic, since they're running out of money, but that one doesn't burn me as much as the Vical one, because you know, we weren't doing the AAV, but there have been a couple of situations like that, I guess it happens.

JONES: Has Viagene ever benefited from any of these?

JOLLY: I'm sure we did, I can't think of any specific examples. The other thing that comes to mind is the tk stuff, the prodrug activation technology which Chiron and Viagene basically started, independently, we both went to see Burroughs-Wellcome, because they're a natural partner for that stuff, because they make acyclovir and they're into purine and pyrimidine drugs, and both of us think that there was some hanky-panky there, but anyway...

JONES: When you were talking to Vical, was that when, I guess Doug Richman was on the SAB here?

JOLLY: Yeah, he was on our scientific advisory board at the beginning, and he was also a founder at Vical, so eventually, actually we kept him on for quite a while, I don't remember exactly when we finished, actually we talk to Doug, and actually he's now a consultant to us again, but basically about HIV rather than the DNA stuff, which is not really his shtick, you know.

JONES: There are a lot of high profile gene therapy people here, Ted Friedman, for instance, in San Diego…

JOLLY: They've all been our scientific advisors at one time or another, with the exception of Carson, I guess.

JONES: So, there is a lot of back and forth with the academic community, and for instance, what kind of publishing policies do you have here at Viagene, well, maybe it's changed now, but…

JOLLY: No, actually, the policy is to publish as much as we can and the funny thing about it is, I've interviewed lots and lots of people for jobs here, and people who come straight out of academia always ask me that question, 'Well, what's the policy for publishing because I really want to publish.' And so the answer always is, 'Your job is to publish, which helps both you, in terms of your personal prestige, which will help the company, because then you can go talk to people and they'll know who you are, which helps the company's prestige. And of course, we'll want to file patents on something, but usually that's not an impediments to, even timewise, as long as we do things in an organized fashion, for getting things published.' And the funny thing is, like you have to whack people over the head with a baseball bat to get them to write papers up, because when you get into a commercial setting, it's not the only thing you have to do, it's not your only product, it's only one among a number of things that you're supposed to do, and in fact, in the grand scheme of things, if you don't publish something, there are often no immediate repercussions, and so actually, we end up giving people goals and saying, 'You've got to write two papers this year,' and they go, 'Oh, no! I don't want to do that.' So, it's funny, everybody pays lip service to that, but to getting people to write once the absolute imperative that this is all you do, this is your only product, this is what you're going to be measured by, 100%, once that goes away, no one likes to write to papers.

JONES: What was Brad Gordon's role, and how long was he involved?

JOLLY: He was chief skinflint. He won't mind me saying that, he'd be proud of that. Brad was originally a venture capitalist that Harry and Paul had met, and I met him as a venture capitalist as well, one of the times I came back from France, in some big office downtown. I think I still have the draft business plan that he'd help them write. So Harry and Paul were busy raising money for Gensia, so they'd gone to see him about that, but they'd also talked to him about the gene therapy piece that they were

including with Gensia. And I guess Brad, at that time, was kind of fed up with being a venture capitalist, as he put it, I think he wanted to invest more of himself into something. So when Gensia was up and running, after about a year, in '87, when they wanted to put a starter organization together, I can't remember if Brad was employee #1 or #4, or what, but anyway, he was hired to do the business part, to basically be the nucleus for the business organization, to do everything. You know, Brad's ambition at that time, I know, was to do corporate development. I guess it hasn't totally worked out, but you know, he had the financial understanding to organize that, and form a business nucleus, which he did. He did a good job doing that. And so, when I say chief skinflint, he was always like, you may have heard this story from Brad, but when we were going to buy a refrigerator, he would always insist that we bought it from Cousins' Warehouse, which is down on Pacific Highway, because you could always get a refrigerator for six hundred bucks there. Sometimes that was suitable and sometimes it wasn't. So, when it wasn't suitable, there was always this big giant to-do to persuade him to buy a real refrigerator. And the same was true of Xerox machines. I think we probably spent more time deciding which Xerox machine to buy, and more salary money, than we actually saved buying the machine. We still have the Xerox machine, so I guess it was a good one.

JONES: And how long did he stay?

JOLLY: Brad stayed, it must have been about '93 or '94, after a lot of people left. I mean, what happened was, Brad didn't have the experience to take, I mean, we had made a good hire in Jeff Works, who was the ex-CFO of Cetus, but he was someone who had been through public offerings, and Brad hadn't, so I guess, when Jeff was hired, then, to some extent, Brad was less essential, and he probably saw that. I mean, there were plenty of things for him to do, but I think it was the right thing for him to do, to move on.

JONES: What's he doing now?

JOLLY: He's CFO at Signal, and he's managing their money in the same way, I hear.

JONES: Well, the last time you told me that Greg Phelps was the 'fall guy' when one of the financing rounds wouldn't come together. What exactly were the problems at that time? Were they problems with milestones, technical problems? A matter of business strategy? Or the implementation of strategy?

JOLLY: I think there were a couple of issues. We were always on the, well, there were several issues that kind of came together to make that not work. I was going to say, we were never on the leading edge of those companies with new ideas on how to raise money. We were sort of on the tail end of the 'selling the dream' type stuff. So, it had been hard for us. It's never to easy to raise money, anyway, but I think Greg, you know, we really followed what the prices of the different rounds of venture capital funding were, and used that as a measure of our progress, and so, I think one thing that Greg probably regrets is he probably went out at too high a price originally. He probably did that in response to expectations of people in the company who needed to feel that they were making progress, and so too go out at a price that was not very different from the previous round, or not a substantial drop from the previous round. Retrospectively, that probably was a mistake, and what made it happen there was we went to talk to like one gazillion venture capitalists and it was tough to get money, and then, you know, the famous, the way to describe it is the story got stale, so even when the price went down, it was like, 'Oh, we've heard it before,' that kind of thing. And also, just the climate for venture capital at that time when we were trying to close Series D was not a good time. A lot of them were not making money, going out of business and all that kind of stuff. So, it was a tough time to get money out of venture capitalists. And so, it was a combination of those things, and, so I don't think it was particularly his fault. Some mistakes were made, as they say, and certainly they weren't all his own mistakes, but in a sense, they just needed to show that the company wasn't the same, you know, we're making changes, and all that kind of stuff. I think that's kind of what happened.

JONES: Is that when Steve Mento came in?

JOLLY: No. Greg got given the boot about, let's see, in June of 1990, and I actually remember it. I remember he was off to see David Hale, 'I'm off to see my boss,' and he had no clue that that was going to happen. But anyway, so then David appeared and we all swore fealty, you know, 'I believe,' and then there was a guy named Mark Lostrom who came from Seattle. He was a consultant, and he wanted to do corporate development as well, and he actually came from the company that Gene Dreams is about, Genetic Systems.So he had been a tech for Nowinski, who was one of the founders. I asked him if he was in the book. He said, 'I looked through it, and thankfully, I think my name was only mentioned once.' So, he had made money doing that, and Mark knew more than we did about biotech and product development, but not a great deal more, but he was like the only guy around, so he

was sort of the interim CEO. David was supposedly the real CEO, but Hale was never around. So, basically Lostrom ran the company while they looked for a replacement, and we went through a number of people who came around, and Bob [Abbott] had been with NeoRx in Seattle, which was a company he helped found, and then he fell out with, what's the guy's name? Bruce Carter, that's right, and I'm not quite clear about how he got booted out of NeoRx, but he left NeoRx not quite of his own volition, and I know that he wasn't necessarily the Board's first choice, but he wanted to do it, and he basically talked them into it, and so Bob became CEO in about January of '91. Is that right? Yeah, that's right, and we then, two months later, signed the deal with Green Cross, and you know, that original deal was done in part, there were a lot of reasons it was done, but one of them was that Phelps knew Nishida who was on the Board of Green Cross, and he had done a deal with them before as part of Xoma Genetics, so that's kind of how we got in the door basically, but anyway, Bob got to sign the deal and sort of become an instant expert on Japanese deals. Then Mento didn't come on board until approximately a year after that, I think February of '92.

JONES: Was the Board involved in bringing him in?

JOLLY: Well, we decided, I mean, Bob decided, and he was right, that we had tried to build some kind of product development capability, but we didn't know terribly a lot about what we were doing, and actually, I don't know if he made that decision, but I think it was Bob, that we needed, Bob made a lot of large-scale right decisions in my opinion. He's a character, but I have a lot of respect for him. He decided that we needed a real product development and potential manufacturing capability, and to do that, we had to import someone who had done it before. So, we set out on a search, and I'll always remember talking to Mento the first time, and basically Bob had to enlist me in that, because I was going to report to that person, so, you know, I bought into that because I understood that it was true, and so, we went to talk to a bunch of people, and all of us went to talk to Steve the first time in some restaurant in Pearl River, because he worked for Lederle, and he was like not interested. And we came away thinking, 'The guy's got no energy.' He didn't say anything, really. So, it's funny actually, because today is his going away party, so maybe I should tell that story. Because you know, he's resigned.

JONES: I didn't know. When was that announced?

JOLLY: Last week. He's going to become CEO of a company called IDUN, here. So, Kiery Kowal and I are going to report to Rusty Williams up in Emeryville, and run the place here. Anyway, we came back, but he looked on paper like possibly one of the right people, and Harry decided that he was a good person, so Harry, Harry Gruber, basically persuaded him that this was the job for him. You know, when Harry gets something in his head, you know, it's like having a bulldog around your ankle. And he basically got Mento out here, and then Mento got interested, and the rest is history, as they say. So then, it was like, 'The house has to be this big….' that kind of stuff. But Steve came out, and, in effect, as Kowal once said to me, 'You know, Mento was made for biotech.' He's just the right kind of guy for doing this stuff.

JONES: What are the qualities that are necessary?

JOLLY: Well, you know, he's a good leader. He's scientifically very smart. I mean, he may not know really the science, but his judgment is good. And he's willing to make decisions on partial information. You know, he's good at most of that stuff. He cares about the organization, the people in it. He tries to make sure that people are treated fairly, all that kind of stuff. So, he has the management part and the science part, and they're both strong. So, I would expect IDUN to do pretty well. You never know. And for us, he knew product development, and he also hired Kiery Kowal, and Kiery is someone who would never have come here if it hadn't been for Mento.

JONES: He came from Big Pharma?

JOLLY: He came from Lederle as well. I've never actually been able to figure out whether Kiery was Mento's boss, or Mento was Kerry's boss, or whether they were side by side, because [?] But he's a product development/manufacturing guy, absolutely what you need in my opinion. He has lots of experience. It's just really tough to get those guys out of Big Pharma and into biotech companies. But that was key. It's always tough in organizations making that transition, from being, I mean I've done it enough, but you know, things change and any start-up company that's successful, it always starts with the research piece, and then kind of grow off of it. And that's tough for the people in research. At one time, you're the center of attention, and then you're not. And then you're very definitely not, because, you know, you don't have the potential to make money. That was tough for everyone, and I think I played a part, and the management did a great job of selling that whole idea to the people in research, and we were able to grow product development and

manufacturing capability in relative harmony, let's put it that way. And Mento was a good guy to have around to do that.

JONES: One of the things that Harry Gruber cited for the problems at Gensia, one of the things that he was unhappy about consistently over the years, was that they were doing too many things, they over-diversified, and he said that Viagene was more narrowly focused, and maybe too narrowly focused.

JOLLY: Well, it goes in cycles, yeah, it's a matter of balancing, but it does go in cycles. For example, just that product development piece, we needed to do, when we were at the first clinical trial, we decided that we needed to do a whole bunch of monkey studies, and we needed to create the capability, because the first trial was going to be with ex vivo fibroblasts, we had to create that capability to grow those fibroblasts in some kind of controlled way, and we didn't have the personnel to do that. I mean, we consistently asked people to stop what they were doing and do this, because the company needs you to do it, and people always responded, and they responded because gene therapy is fun. As I probably said before, even QC for gene therapy is fun and new. So, people had to really narrow down what they were doing in those situations, and we never had enough money to afford to do both that piece and the sort of next new bit of technology development, but I think that's always true in biotech companies, you always get to that stage, and I've talked to a lot of people in biotech companies and they always say, 'You've got to put your head down and just keep doing that stuff, because it's the only thing that will get you through to the next piece of money.' And we were able to do that and still keeps our minds alive. So, I think that was relatively successful, but I would agree with Harry that there's lot of other, and we're still doing that balancing act, because I know that the next, some of the things that we should be working on, the next technology issues, we're not spending as much effort as we would like. Why is that? Well, because we have a limited budget, and we're trying to make products and all that kind of stuff. There's certainly a danger in trying to do too many things all at the same time. You're more likely to survive if you're narrowly focused than if you're not, but of course, the question is what comes out at the end. But, so far so good.

JONES: What were the circumstances surrounding the Chiron sale, and how has that changed things around here?

JOLLY: Well, the background to that is, in the latter of half of '93, we had about eighteen months money, from about July, something like that, approximately, at the same kind of burn rate, and it was like Series D all over again, we had been in registration forever and the window closed the first time in 1992. The judgment was that we needed another Big Pharma deal or big company deal to get the IPO done. And the two possibilities that sort of emerged were Chiron, and Chiron interested us because Bob Ralston, who worked there, was interested in gene therapy, and wanted to use prodrug activation technology, he did a patent search and found that he had a pretty good potential patent position, nothing issued yet, but filed. So, they came to see us, and we talked and eventually, so that's the origin of Chiron's interest. And so, the other company that we had the potential to do a deal with, we thought, was Burroughs-Wellcome, actually, around the same kind of technology. But the only one that could really move fast enough was Chiron, you know, Burroughs-Wellcome was just too big, because we needed to go public, we needed the money, because once you get down to that years' worth of money, the sharks start to circle, which is what's happened to Targeted Genetics, right now. So, there was all this toing and froing and we signed the deal with Chiron, a cute deal, actually, I don't know quite who designed it from Chiron's point of view, because now I'm part of Chiron, I figure we should do that kind of deal with everyone. The deal was they took stock, bought about $12 million worth of stock, and then there was a deal for us to do joint projects with a joint fund of $24 million, but we would spend the firs $12 million and they would spend the second $12 million. So, although there was no real tie there, in writing, basically they were giving us $12 million dollars and we would spend it on the joint research, but it came out of their equity line, so it's an asset not a debit, and then they would have to worry about whether they'd have to spend the $12 million. When you look at it, you know they were thinking, you know, we could buy or not buy at that point. And then, they had about 18 or 19 percent of Viagene. At that point, retrospectively, the die was almost cast, because it's hard to sell yourself to someone else for major projects when Chiron owns 20% of you, just under 20%, as we found out in the next year or so. So, we signed the deal, and there were a couple of projects, but the centerpiece was this thing around prodrug activation, which is, actually, it's kind of funny in retrospect. Basically, it was totally dysfunctional project groups because no one had thought about the fact that two companies always do things different ways, you know, their willingness to take risks in a particular area, or how you make decisions, all that, they're naturally different, and Chiron's was certainly different from ours, and you know, they were trying to be, to act like Big Pharma, and

we were still gun slinging as it were, and then, I was on that project team and it did not work. I mean, there was no mechanism for resolving the deadlocks, and also, there were some personality conflicts at a higher level. I guess Rusty Williams was hired by Chiron, I guess a few months before the deal was actually signed, I guess, actually, it was eight months, but then he broke his leg or something, and he was on crutches and wasn't able to do anything. Then, he came from academia, and he and Bob, I don't think were favorites of each other, and so, there wasn't a good method of conflict resolution, and then, besides that, the other problem was that the deal was written in such a hurry, between us and Chiron, that there were things that didn't make sense, you know, it had been altered over here, but a piece over there hadn't been altered, so this thing would refer to something back here, but it wasn't there, and so, what did this deal mean? And we spent a whole year basically, I mean, most of us weren't parties to that, I think most of it came from, I think, between Bob and Rusty, which is, they spent a whole year discussing, like, 'What I think it means it this,' and 'No, no, I think it means this.' So, there were two issues, nothing much was happening on the tk front, and no one could agree what the agreement meant, and so, I think, Chiron, and this is just my take on it, had sort of the options of we buy or we walk. And luckily for us, probably, they chose to buy, and that was kind of an on again, off again thing, and you know, in retrospect, we didn't have to get bought, because the market improved, we could have done another run at the funding, but we didn't know that at the time. When all this was going on, the market was on the rocks, especially for biotech. You didn't have a chance at raising money. Of course, immediately when we got acquired, the market improved. So, anyway, there was some to-ing and fro-ing and then, there are various stories of the motivation of the board for doing this, but anyway, they decided they wanted to sell. They were still mostly VCs, so the story is that they weren't too crazy about Bob. Harry's probably told you that story. Anyway, they were VCs, they wanted their money, so this was a way to get it, and I think Hale actually did the deal. He's the one who decided, 'We've got to do this deal.' And there was some dicking around, but eventually they did it.

JONES: What was your personal feeling about the company now being part of...

JOLLY: Well, I guess I understood, by then, that if you wanted to, that gene therapy is applied science, if you want to find out if it works, you have to be in the clinic. Being in the clinic is expensive, and there's no way you can raise that money, you can raise that money on Wall Street, but you've got one shot at it, and then you're probably screwed. So, your chances of, the first thing, hitting, are not terribly high, so

that's a very dangerous way to get money to do clinical trials, and then the venture capitalists don't have access to that kind of money. You have to borrow from pharmaceutical companies, which effectively is what Chiron was. And so, the only place you're going to get it is from pharmaceutical companies. We actually had a partner in Green Cross that was prepared to go forward and pay for it, without us owing them, but that's usually not the case. We needed more than that, otherwise we'd have been an HIV therapeutic, a one product company, and so, it's sort of inevitable that, you know, there's Amgen, and that's it. And they just got extremely lucky. It just didn't happen with gene therapy, so…

JONES: And you're happy with Chiron? I mean, Chiron is not a giant…

JOLLY: Well, the good thing about being bought by Chiron is that they are science-driven, and sometimes I think that's like, you know, there are two kinds of CEOs, there are the CEOs who really understand the technology, and there are the CEOs who don't care and who are only interested in the marketing, the business guys, and it's hard to decide which kind is the better, you know, for the obvious reasons. If you're the R&D guy, the marketing business type CEO just wants to know when you're going to do it, and how money it's going to take, and you better get it done. But after that, you're pretty much on your own, whereas the one who understands the science wants to get involved, so, that's the good and bad parts. And the same thing is true of getting taken over by a company, so you can have a science-driven company like Chiron, but then they want to know everything and they want to pass scientific judgments and everything, but at least you have the feeling that they're trying to understand, trying to make decisions based on that, or you get taken over by a giant pharmaceutical company which doesn't have a hope in hell of making science-driven decisions, and then they become arbitrary. I've only done one, so I don't know whether the other kind is better or not. I have a feeling that the Chiron kind is probably better, just looking at what's happened to some of the other gene therapy companies that got bought by straight pharmas.

JONES: Over the years, how hard how you worked at this personally?

JOLLY: Extremely hard. Most of the time, well, it's like research, 10% fun and 90%, whatever it is that Thomas Edison said. It's the same for this, but now I've got my personal investment in the whole thing, so, I mean, Viagene was a blast. I mean, that was probably the most fun I've ever had in the world, actually. Just because exciting

things were happening, but all this crazy stuff would happen, too, and you'd just have to deal with it. I mean, I wouldn't have missed that for the world. But you can get misty-eyed over that, mistaken, because you always forget the bad stuff. You know, there was the usual set of bad circumstances. We never ran out of money, it didn't quite come to that, so I can look back and laugh. The experience with Chiron is a little different, but it's, well, I mean, my goal, right now, is to make sure that I'm part of the first gene therapy product that gets marketed. That's what I want to do. My job is really to fill the pipeline, but I can stay involved and be part of it. So, I mean, that's really exciting. There's much more, you know, with Chiron, there's many more people to talk to in order to get agreement about doing things, and Chiron doesn't have a strong formal organization, so it's not always clear sometimes who you should talk to, but even the companies that do have strong formal organizations, there's usually the hidden one, as well, so you have to figure that out, anyway. And, you know, Chiron wants to do gene therapy, there's no doubt about that, so that's good, and they've got the money to do it, so I mean, I'm happy with that.

JONES: You're confident that you'll be able to put out the first gene therapy product? Are you getting close?

JOLLY: I think we've got, well, you know, nothing's a surefire bet. We've got a couple. The HIVIT program, I think that has a chance of working. Not everyone around here believes that, but I think it has. If that were to be successful, it could easily be the first gene therapy product. We also have this graft versus leukemia program which is no big secret, it's an ex vivo program. The cute thing about that is that it works, we know it works, because it's been published in Science.

JONES: It has been, or will be?

JOLLY: It has been.

JONES: Whose name is on it?

JOLLY: The work that's published, the lead author's name is, a guy named Bordignon, he's in Italy. But the idea there is after allogeneic bone marrow transplant, or, I mean, it's kind of an arcane application, but the cute thing about is there's nothing there that's not possible, and it works. So, it could be a product, we've just got to do the product development piece. And the idea is that you do allogeneic bone marrow transplants into lymphoma leukemia patients and people have discovered

that if you do that, you've got a lot of graft versus host disease [GvHD], so then it depleted the T-cells out of the marrow, and you then get better engraftment, but then you get more recurrence of the tumors. And they figured out that if you give them T-cells as well as the marrow at a slightly different time point, you could sort of get donor T-cells to destroy some of the lymphoma, and do a little bit of graft versus host and the cytokines made were good for the engraftment, but if you give them too much, you get graft versus host disease and the person died. And then the next fix on top of that is when you put the lymphocytes in from the donor into the patient, you put the tk gene in, so that if you get graft versus host disease, you can eliminate the T-cells by giving ganciclovir. So, it's somewhat baroque, and the first time I heard it, I went, 'Forget it.' But it all works. It's been published. So, we can make the vector. We have proprietary rights to tk. We have to share some of those rights with RPR Gencell. We signed a deal with Baxter at the beginning of the year to get the T-cell technology, that's basically done. And clinically, it works. So all you've got to do is put it all together. There's nothing there that can't be done. There's no technology jump. It works. I don't know how well it works, but it works. And that has occurred to other people as well, so the group in Milan, the Italian group is, or was, relatively independent, it was supported in some work by Boehringer-Mannheim, which just got bought by Hoffman-LaRoche, so there maybe they're a competitor now, after all, I don't know. But they were just an academic group doing it, at that time, and then GTI, that's a program to do that, they started doing it in France, the [?] so it's occurred to other people as well. But we have actually all the pieces, so now it's sort of a race to get it done. And if HIVIT is not successful, then that's probably going to be the first gene therapy product, unless we get blindsided by something.

JONES: But you still have to go through…

JOLLY: The approval process, yeah.

JONES: Which would still be five, six years?

JOLLY: Yeah, I guess we're trying to get it done shortly after the beginning of the new century, let's put it that way. So, 2002, something like that. I mean, if HIVIT hits, it could probably be even sooner, but the question is whether it's really going to.

JONES: How far along is that?

JOLLY: Well, we have a trial that has the potential to allow us to go for accelerated approval. We have two Phase II trials, actually. One, we'll have the data in quarter three or quarter four, this year. It was a two hundred patient trial originally, but the trouble with that one was it treats in the context that doesn't exist anymore, because all of the HIV patients are jumping to triple drug therapy. So, the second trial treats in the context of triple drug therapy, and we'll see what happens there. There were some, as they say, interesting trends in the interim analysis of the first Phase II, so we'll probably have a pretty good before this year is up whether we're wasting our time or not with the second one.

JONES: So, this is a critical juncture. Do you spend a lot of time worrying about the outcome?

JOLLY: Actually, no. What you spend your time worrying about is whether you made the right decisions up front, and that things get run, mechanically, right. And with clinical trials, you just can't worry about them. It's like you just switch off your brain for a year until you get to see the data, so, I mean, it's not true that I don't worry about it, but there are lots of things to do there, and you have to keep the product development going, to match the clinical progress of the product, because the FDA is going to ask us lots more questions about, 'What is this stuff?' if we're going for product approval rather than trying it in Phase I. So, we have to try to anticipate those questions.

JONES: What's your view on what happened with the clinical trials of the adenosine compound at Gensia? I have had people tell me that the stuff worked, but they just screwed up the clinicals.

JOLLY: Yeah, you know, I don't know the details of that at all. What I do know is, I think, I don't know if you know this is true, but they bought that compound from Japan, and I think that Japanese company had run trials on it already and had gotten, I don't know how big those were, had got sort of marginal responses. So my guess would be that you could probably run a trial to get approval, but I don't know whether it would sell or not. So, you know, the problem about Gensia, in my opinion, was the strategy of the whole company. I mean, it's easy to say in retrospect, but it's tough building a company on one or two products, because if they don't work, you're screwed. So, it's easy to raise initial money on them because people love the story because they can see how it's going to work, it's going to go boom, boom, boom,

without any of this messy technology development here, where I don't know whether it's going to work or not. I can see all the steps and I understand that, and all right, I'm willing to risk my money. So it's easy to raise the money initially in that sort of situation, but there are two drawbacks. One is that you don't have any back-ups, so they didn't have any other compounds, and the other is that you're spending money on clinical trials right away, and it's expensive, so you're going to blast through the money. And those were the two drawbacks that Gensia had, and that's exactly what they did, I mean, it's easy to say in hindsight, but they blasted through the money, and they didn't really have anything else that was ready, that was close behind. They had lots of other stuff they were trying to do, but they never sold that as a story, in my opinion. They were always selling them on those lead products. So, Viagene was the opposite. We were selling the technology, which makes, you know, the first round is easy, and then people go, and I'll always remember, it was always, 'Have you done any animal experiments? Have you injected chimpanzees? Have you started clinical trials yet?' And it was always like, 'Well, we haven't done that one yet. We just did the last one.' But, in the end, there's more to fall back on, in terms of, if this doesn't work, we can do this or this.

JONES: But there were a lot of people who were involved with Gensia, that were also involved with Viagene, at the board level.

JOLLY: Yeah, it's interesting. It's interesting that way. At the time, I didn't really understand the decision to spin out Viagene, but that was absolutely the right decision, because the two pieces couldn't have coexisted together, I don't think. So, that was the right thing to do?

JONES: Do you have any other good anecdotes? Any other funny stories?

JOLLY: Ah, funny stories. Well, we used to name the monkeys after the venture capitalists, some in particular, but, yeah, there are probably some I shouldn't tell. I remember when we were going to do the Green Cross deal and Phelps was still around, and we were looking for a commitment from them, they were going to send us a fax telling us whether they wanted to go forward or not, basically whether they were serious, so we held an all-night fax party, and we just sat in the fax room and around the fax room, drank, ate, and wore party hats, well, we didn't wear the party hats until the fax came through. And then when the fax came through, we drank

some more. That was fun. That was Phelps' idea. It was a good idea. Let's see, there are all the Bob Abbott stories.

JONES: There are a lot of those?

JOLLY: Yeah. Bob, when we went traveling with him, he used to, he loved, he really liked traveling, and he would spend time figuring out how to go to more than, basically, what he liked best in the world was to go to at least three cities in one day. That gave him a feeling of satisfaction, I think. So, he would spend on airline routes, trying to get inexpensive flights and get the maximum amount of business done in a day, I guess that's how he was looking at it. So, it was exhausting to travel with him. But the funny thing was, when you went traveling with him, he always wore a suit, and he carried this plastic bag, and that was it. And the speculation was what was in that plastic, and I always meant to ask Bob that, but I never did. One hopes it was underwear. We used to go partnering in Japan, because value in those days was whether you had a Japanese partner, and I'll always remember being in a taxi with Steve Mento and him, and Bob, it was really funny because we had different projects, and you know, you wanted to present things in different ways in different situations. And Bob was really good at this is. He would say, "You know, I think we need some herpes, some product development, and some hepatitis." And you know, Steve and I would start shuffling sheets, and you know, we got good at that.

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.