Regional Oral History Office
The Bancroft Library

University of California
Berkeley, California

Program in Bioscience and Biotechnology Studies

JAMES M. GOWER:
BUSINESS DEVELOPMENT AND MARKETING STRATEGY AT GENENTECH, 1982-1992

Interviews Conducted by
Sally Smith Hughes
in 2004

Since 1954 the Regional Oral History Office has been interviewing leading participants in or well-placed witnesses to major events in the development of northern California, the West, and the nation. Oral history is a method of collecting historical information through tape-recorded interviews between a narrator with firsthand knowledge of historically significant events and a well-informed interviewer, with the goal of preserving substantive additions to the historical record. The tape recording is transcribed, lightly edited for continuity and clarity, and reviewed by the interviewee. The corrected manuscript is indexed, bound with photographs and illustrative materials, and placed in The Bancroft Library at the University of California, Berkeley, and in other research collections for scholarly use. Because it is primary material, oral history is not intended to present the final, verified, or complete narrative of events. It is a spoken account, offered by the interviewee in response to questioning, and as such it is reflective, partisan, deeply involved, and irreplaceable.

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It is recommended that this oral history be cited as follows: James M. Gower, "Business Development and Marketing Strategy at Genentech, 1982-1992," an oral history conducted in 2004 by Sally Smith Hughes, Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 2006.

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James M. Gower

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Genesis of the Program in Bioscience and Biotechnology Studies

In 1996 The Bancroft Library launched the forerunner of the Program in Bioscience and Biotechnology Studies. The Bancroft has strong holdings in the history of the physical sciences--the papers of E.O. Lawrence, Luis Alvarez, Edwin McMillan, and other campus figures in physics and chemistry, as well as a number of related oral histories. Yet, although the university is located next to the greatest concentration of biotechnology companies in the world, the Bancroft had no coordinated program to document the industry or its origins in academic biology.

When Charles Faulhaber arrived in 1995 as the Library's new director, he agreed on the need to establish a Bancroft program to capture and preserve the collective memory and papers of university and corporate scientists who created the biotechnology industry. Documenting and preserving the history of a science and industry which influences virtually every field of the life sciences and generates constant public interest and controversy is vital for a proper understanding of science and business in the late twentieth and early twenty-first centuries.

The Bancroft Library is the ideal location to carry out this historical endeavor. It offers the combination of experienced oral history and archival personnel and technical resources to execute a coordinated oral history, archival, and Internet program. It has an established oral history series in the biological sciences, an archival division called the History of Science and Technology Program, and the expertise to develop comprehensive records management and to digitalize documents for presentation on the Web in the California Digital Library. It also has longstanding cooperative arrangements with UC San Francisco and Stanford University, the other research universities in the San Francisco Bay Area.

In April 1996, Daniel E. Koshland, Jr. provided seed money for a center at The Bancroft Library for historical research on the biological sciences and biotechnology. And then, in early 2001, the Program in Bioscience and Biotechnology Studies was given great impetus by Genentech’s major pledge to support documentation of the biotechnology industry. Thanks to these generous gifts, the Bancroft is building an integrated collection of research materials--oral history transcripts, personal papers, and archival collections--related to the history of the biological sciences and biotechnology in university and industry settings. A board composed of distinguished figures in academia and industry advises on the direction of the oral history and archival components. The Program's initial concentration is on the San Francisco Bay Area and northern California. But its ultimate aim is to document the growth of molecular biology as an independent field of the life sciences, and the subsequent revolution which established biotechnology as a key contribution of American science and industry.

Oral History Process

The oral history methodology used in this program is that of the Regional Oral History Office, founded in 1954 and producer of over 2,000 oral histories. The method consists of research in primary and secondary sources; systematic recorded interviews; transcription, light editing by the interviewer, and review and approval by the interviewee; library deposition of bound volumes of transcripts with table of contents, introduction, interview history, and index; cataloging in UC Berkeley and national online library networks; and, in most cases, digital presentation at http://bancroft.berkeley.edu/ROHO/projects/biosci.

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University of California, Berkeley
November 2005

ORAL HISTORIES ON BIOTECHNOLOGY

Program in Bioscience and Biotechnology Studies
Regional Oral History Office, The Bancroft Library
University of California, Berkeley

Paul Berg, Ph.D., *A Stanford Professor's Career in Biochemistry, Science Politics, and the Biotechnology Industry*, 2000

Mary Betlach, Ph.D., *Early Cloning and Recombinant DNA Technology at Herbert W. Boyer's UCSF Laboratory*, 2002

Brook Byers, *Biotechnology Venture Capitalist, 1970-2006,* 2006

Herbert W. Boyer, Ph.D., *Recombinant DNA Science at UCSF and Its Commercialization at Genentech*, 2001

Ronald Cape, M.B.A., Ph.D., *Biotech Pioneer and Co-Founder of Cetus,* 2006

Roberto Crea, Ph.D., *DNA Chemistry at the Dawn of Commercial Biotechnology*, 2004

James Gower, *Business Development and Marketing Strategy at Genentech, 1982-1992,* 2006

Donald Glaser, Ph.D., *The Bubble Chamber, Bioengineering, Business Consulting, and Neurobiology,* 2006

David V. Goeddel, Ph.D., *Scientist at Genentech*, *CEO at Tularik*, 2003

Herbert L. Heyneker, Ph.D., *Molecular Geneticist at UCSF and Genentech, Entrepreneur in Biotechnology*, 2004

Keiichi Itakura, *DNA Synthesis at City of Hope for Genentech*, 2006

Irving S. Johnson, Ph.D., *Eli Lilly & the Rise of Biotechnology*, 2006

Thomas J. Kiley, *Genentech Legal Counsel and Vice President, 1976-1988, and Entrepreneur*, 2002

Dennis G. Kleid, Ph.D., *Scientist and Patent Agent at Genentech*, 2002

Arthur Kornberg, M.D., *Biochemistry at Stanford, Biotechnology at DNAX*, 1998

Laurence Lasky, Ph.D., *Vaccine and Adhesion Molecule Research at Genentech*, 2005

Fred A. Middleton, *First Chief Financial Officer at Genentech, 1978-1984*, 2002

Diane Pennica, Ph.D., *t-PA and Other Research Contributions at Genentech*, 2003

Thomas J. Perkins, *Kleiner Perkins, Venture Capital, and the Chairmanship of Genentech*, *1976-1995,* 2002

G. Kirk Raab, *CEO at Genentech*, 1990-1995, 2003

George B. Rathmann, Ph.D., *Chairman, CEO, and President of Amgen, 1980–1988*, 2004

Regional Characteristics of Biotechnology in the United States: Perspectives of Three Industry Insiders (Hugh D'Andrade, David Holveck, and Edward Penhoet), 2001

Niels Reimers, *Stanford's Office of Technology Licensing and the Cohen/Boyer Cloning Patents*, 1998

Arthur D. Riggs, *City of Hope's Contribution to Early Genentech Research,* 2006

William J. Rutter, Ph.D., *The Department of Biochemistry and the Molecular Approach to Biomedicine at the University of California, San Francisco,* volume I, 1998

Richard Scheller, Ph.D., *Conducting Research in Academia, Directing Research at Genentech*, 2002

Robert A. Swanson, *Co-founder, CEO, and Chairman of Genentech, 1976-1996*, 2001

Axel Ullrich, Ph. D., *Molecular Biologist at UCSF and Genentech,* 2006

Daniel G. Yansura, *Senior Scientist at Genentech*, 2002

William Young, *Director of Manufacturing at Genentech*, 2006

Oral histories in process:

Paul Berg

Stanley N. Cohen
Marcy DarnovskyWilliam Green
Daniel E. Koshland, Jr.
Donald Reed
William J. Rutter
Mickey Urdea

Pablo Valenzuela
Keith R. Yamamoto

Interview History—James M. Gower

Jim Gower was interviewed for the oral history series on Genentech to document his ten years (1982-1992) at the company in business development and pharmaceutical sales and marketing, ultimately as a senior vice president. Coming from American Hospital Supply Corporation, he was among the few in the pharmaceutical industry willing to take a leap into the untested waters of commercial biotechnology when an industry did not yet exist and young companies such as Genentech were struggling to get off the ground. In these pages, Gower explains why he found enticing the job offer from Bob Swanson, Genentech's young CEO, despite the personal and corporate risks involved. He also describes his part in the launch of human growth hormone, the company's second product (after human insulin), and in controversial decisions regarding tissue plasminogen activator (t-PA), the company's "[blood] clot buster" and supposed phenomenal moneymaker. As a direct participant in Genentech's acquisition by Hoffmann-La Roche, Gower discusses the negotiations and complex buyout. All this and much more occurred against a background of Gower's effort in shaping and refining the company's business goals and marketing forecasts.

Two interviews were conducted in Gower's office at Rigel Pharmaceuticals in South San Francisco, where since 1996 he has served as CEO and board chairman. He genially responded to questions, emphasizing the importance of his experience at Genentech in his current role at Rigel. He diligently edited the interview transcripts, concerned that the facts and English be correct. By agreement between the Bancroft Library and Genentech regarding the oral histories Genentech supports, its legal department received transcripts of this and all other oral histories it supports, to review solely for current legal issues. As in all instances to date, no changes were requested.

The Regional Oral History Office, a division of the Bancroft Library, was established in 1954 to record the lives of individuals who have contributed significantly to the history of California and the West. We are pleased to have this oral history join the collection in the Program in Bioscience and Biotechnology Studies.

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August 2006

Interview 1, July 29, 2004]

[Begin Tape 1, Side A] ##[1]

Hughes: Please start back with your parents and tell me where they came from and what they did.

Gower: I can do that. They were both from a small town in rural Tennessee called Springfield—the closest town is Nashville. They had grown up there, and their families had lived there for quite a while. My mother Dorothy was, until she retired, a secretary-administrator at the local high school, had been virtually her entire career. My dad James ran the Middle Tennessee Farmers' Cooperatives, which provided supplies for the local farmers. They had met at college, at the University of Tennessee, back in the forties.

Hughes: Do you have brothers and sisters?

Gower: No, I'm an only child.

Hughes: Tell me a little bit about your education, where you went to school in your grammar school and high school.

Gower: Went to both grammar school and middle school and high school at public schools in Springfield, Tennessee. Because of the incredibly deluded thought that I could actually play football in the Southeastern Conference [laughs]—even though I was a National Merit finalist, I decided to eschew some of the schools that were better academically and were offering me scholarships. I probably could have played football at, but went to the University of Tennessee in Knoxville, because I had just grown up on that, loved it, decided that that was something I could—-

Hughes: And thought you could play football there, too?

Gower: I was under the incredibly intense delusion that I could play at that level. [laughter] So, since I was "good at math and science," I signed up for a major in aerospace engineering—this is the sixties, remember, we're going to the moon, but we're not there yet. That sounded rational, or at least as rational as you can be at eighteen. Also, I thought, this is great, because I can play football in a major league school. And both lasted almost exactly two years. I was good enough to make the practice team, but came to the delightful understanding in retrospect, but at the time kind of frustrating, that the guy in front of me

1.## This symbol indicates that a tape segment has begun or ended.

playing defensive backfield had made it to the cover of *Sports Illustrated* three times, and [laughter]—

Hughes: It was a little hard to compete.

Gower: I was out of my league. *Completely* out of my league. On the academic side, I was in my league, but I decided that engineering was pretty boring and I had to get out of there. I was beginning to know myself and found out that I had a personality where once I'd done the experiment once, I really didn't want to do it another dozen times, because I knew how it was going to turn out. After my second knee operation, I got out of football, and at about that time, I moved majors. Flirted for a while with going into pre-med, because I still had this fantastic affection for virtually everything scientific, pretty broad tastes, liked it all. And pre-med came the closest, but at the end of the day, in a decision that was probably the first rational decision I made, unlike those earlier ones, I decided I probably wouldn't be all that good with patients. I went into a very odd little discipline called operations research, which is math methods applied to business. It's basically an economics discipline that's sort of half between—or it was in this university—the School of Engineering and the School of Business. That got me into business, and when I got there, I decided that I liked that, and ended up in graduate school there.

Hughes: What appealed to you about it?

Gower: Oh, the fact that it fit a couple of needs for me. One was that you could basically be in business in just about anything, and I knew that that included for me some element of things scientific, because I liked it. And yet, you could be in a world that was much more open and less constrained, not necessarily to the bench or to the lab or whatever, which I was beginning to find with my personality made some sense. As I started working on projects, although this was primarily as a graduate assistant, and I was working with Oak Ridge National Labs on what do you do with this weird—at that time weird—new technology, nuclear magnetic resonance, NMR?

We started focusing on health care applications. It just reinforced sort of all of that mix of, well, there are lots of ways to sort of deal with novel science applied to something I care about doing, but in ways that sort of fit my personality a little bit better than being in a lab or treating patients. And it's worked out okay, at least.

Hughes: So the undergraduate courses kind of led straight into the graduate work?

Gower: Yes. Normally, they wouldn't in business, but I had an offer at the end of undergraduate school to be a graduate assistant for Warren Neel, who later became the dean of the business school, and he was really fabulous. And I really wanted to work with him. So being a graduate assistant and helping out on some

of that research and not having a lot of teaching obligations sort of appealed to me, so I just went straight ahead and got the MBA.

Hughes: And that was in one year, or—?

Gower: Two years.

Hughes: Two years. And then what?

Gower: Well, then you have to do something real for a living [laughter]. I interviewed with a number of different types of companies, but I found myself gravitating more towards health care and pharmaceutical companies, because I sort of always had that bent. I ended up working with a corporation, American Hospital Supply, that's now merged and part of another corporation called Baxter. It was at the time about a $4 billion corporation that was diverse, same sort of concept as a J&J [Johnson & Johnson] but a lot smaller. Everything from bedpans to pharmaceuticals to heart valves to—you pick it. All sorts of divisions, I think thirty-some-odd divisions. And I went to work in the pharmaceutical division.

Hughes: Why American Hospital Supply when there was the whole pharmaceutical industry and the medical device industry to choose from?

Gower: Well, part of it was just luck. I mean, at the time that I was interviewing, there was some interest from a couple of others that were in pharmaceuticals; frankly, I was lucky enough to be asked to interview at the home offices, and I just liked these guys better.

Hughes: I see.

Gower: I also felt that there was some advantage being in diversified corporations, and that you would have a chance to move faster if you were any good at what you did. And luckily for me, that turned out to be true.

Hughes: And did you have a choice for the pharmaceutical division?

Gower: Yes. That's what I picked.

Hughes: You picked it? There was an opening there and that's what—

Gower: Yes, there were four different groups they gave me a choice of. Two of them were more in the sort of supply side, which wouldn't have got into the science at all, although it's in health care. And then one of the cardiovascular device manufacturing groups, which were the guys who invented a fair number of things. They were the first to put artificial heart valves on the market and things like that, so that wasn't unappealing. And then the pharmaceutical group. It was a toss-up between the last two, and I picked the pharmaceutical group.

Hughes: And what was appealing about you to them?

Gower: Oh, I have no idea.

Hughes: Because there can't have been too many young people coming to them with the kind of background that you had.

Gower: Well, that's not true, there were quite a few at that time.

Hughes: With the engineering and the MBA?

Gower: Well, I didn't have an engineering degree; I had two years in engineering.

Hughes: You had engineering experience, the two years.

Gower: Yes; I would say that it was probably more what I'd done in terms of the graduate work, working with new technologies in health care, that got to them more than engineering. Aerospace engineering has a limited appeal in the pharmaceutical industry. [laughter] It's interesting, but—you know. But I think that at that time, in the early seventies, the pharmaceutical industry was in a real growth spurt, based on some of the newer drugs that had followed the antibiotic era of the fifties, which were making most of these groups grow in size and complexity. So I wouldn't want to mislead you; I don't think it was that hard to get a job in the pharmaceutical industry in the early seventies. They were looking for people across the board, in science, in sales and marketing, because they were all growing.

Hughes: What was your first responsibility?

Gower: I took a sales position in Dallas, Texas. I was basically introducing new drugs to the hospital markets, sort of teaching hospitals and the like. Wasn't there all that long; got promoted to be a regional sales manager, and then moved into marketing in the headquarters office in Chicago sometime in the early seventies, around '73.

Hughes: And it appealed to you? You'd found your niche, do you think?

Gower: I really liked the marketing part of the business, yes. It gave me an opportunity to bridge— spent a lot of time with the MDs that were practicing medicine, that would be the potential users of the product, and certainly the researchers that were involved in getting the drugs approved. But also there's the issue which sometimes people see in a positive and sometimes in a negative way— that when you come right down to it, physicians usually have at most one course in pharmacology in their entire medical training. And what do you do with that? How do you get this information across, and what is the best way? What's needed in terms of the medication, and what's the best way to profile your

medication in terms of ways that make sense with the diseases that you're trying to treat?

Hughes: And were you working that out on your own, how to do this, or was there some kind of training that American Hospital gave you?

Gower: Oh, there was training, but when you get to the marketing piece of things, it's more on the job. I mean, sure, there was training, but it's more learning by doing than anything else, as most things are after an MBA as opposed to a Ph.D. There is no such thing as a postdoctoral fellowship; you're doing that while you're getting paid, doing your job. Same concept, but it's applied in a little bit different way.

Hughes: Did you know Bob Byrnes?

Gower: I knew Bob Byrnes; he was my entree into marketing at American Hospital, and I still respect the hell out of him. Great guy, fabulous guy.

Hughes: And you were there for how long?

Gower: For a decade.

Hughes: Well, what about the culture of American Hospital Supply?

Gower: Here is an interesting, but small within the overall context of the corporation, pharmaceutical unit that's in the midst of all these other diversified health care things. And so from the standpoint of everything but meeting corporate financial goals, we were pretty much left alone. I mean, there wasn't this huge bureaucracy that told us what to do. In fact, since this group was one of the youngest, and we were more or less building sort of a niche pharmaceutical company from scratch, a lot of us, not just me, but on the science side, on the medical side, got a chance to do what we would have never been allowed to do in a large pharmaceutical company. American Hospital didn't know any better. We were in our twenties at the time and got a chance to be responsible for a lot of things and cut across a lot of disciplines in a way that you would have never done in a more established pharmaceutical environment.

That was really fortunate for Genentech later on; it obviously wasn't on my mind at the time, but it sure was fun. I knew I was getting the benefit of being in sort of a startup unit but funded by a big, stable corporation, and the combination of those two was not a bad thing. I got a lot of personal advantages in terms of the freedom of what I was able to do, try out, and have an impact on, without waiting my time "in grade," to be able to do so.

Hughes: Then why did it all come to an end?

Gower: It didn't, really; it just moved venues. By the end of the seventies, actually, that division of American was doing quite well, but at that point, my former mentor at American Hospital, Bob Byrnes, was at Genentech. I remember one Friday he called on the phone and said he was in town, and they were talking to someone, and that he had along a good friend of his that was also at Genentech who was a lawyer. His name was Tom Kiley. And, did I have time for them to come by and say hi? I said, "Yeah. We're having our usual Friday afternoon intramural football thing at five-thirty, but come on by." So they came by and we talked for a couple of hours after that. I was pretty intrigued with the crazy idea that you could actually build a pharmaceutical company from scratch based on this new technology of recombinant DNA, which I knew about, but—

Hughes: You did know about it?

Gower: Oh yes, but I had not really given it much thought in a business context. I would do it based on Bob [Swanson] saying it was worthwhile no matter what, but I came out to meet more folk in South San Francisco. They had basically entranced me with the idea that, you know, this is probably crazy, but it's worth taking a look at anyway.

Hughes: And had Byrnes and Kiley come to you initially with the idea of maybe enticing you to come to Genentech?

Gower: Yes.

Hughes: They did.

Gower: Bob [Byrnes] told me later—and Bob Swanson told me later—that for whatever reason, Bob Byrnes felt that I would be involved in, as he described it, sort of my preferred way of working, which was to have a foot in both worlds. I was pretty comfortable working with folk in the labs, talking their language, working with them; I was also pretty comfortable out working with folk in the marketplace. He thought that that was a pretty good fit for where they were going to need to go. It's a good thing he knew me, and it's a good thing he thought that. I'm not sure it's true, but it worked out well. So he had identified me as someone who would potentially be useful in this context.

Hughes: And what was Byrnes' title?

Gower: He was vice president of marketing? I forget exactly, because to be perfectly frank, and this is true of my own titles during those years, I'm not sure they really meant anything. None of us paid a hell of a lot of attention to them. You have to have one, but I do remember clearly that Swanson never actually had a real organization chart until we did the merger. It's true.

Hughes: Is that really true?

Gower: Absolutely true.

Hughes: That long!

Gower: We would occasionally have a semblance of one. HR [human resources] was impossible, could not exist, unless they had something on paper that was an organization chart. But it didn't really reflect anything in terms of how decisions were made, et cetera, and there were many sort of cross-boundary decisions that were made. Various people had a lot of influence on business that weren't in business, and on science that weren't in science. It's kind of one of the delightful things about the place, and that, frankly, was due to Bob Swanson. But Bob Byrnes' title, I believe, at the time I got there, was vice president of marketing. Something like that.

Hughes: Do you think that that fluid system was typical of the pioneering biotech firms? Or was that something that was unique to Genentech?

Gower: Well, I think that fluidity is certainly typical of virtually any startup, not just in biotech. And I think it's certainly true in biotech. I came to find out later, but this is more after a number of years, that there was perhaps more of a difference between the degree to which this was true at Genentech and many of the other biotech startups. I think Bob Swanson really pushed the whole concept of ignoring the boundary lines of areas—having all people understand what was going on in various areas, questioning everything, giving everybody a voice—to the greatest limits I've ever seen stressed anywhere. Sometimes it caused a little unnecessary—it wasn't particularly efficient, let me put it that way. But it had its own genius, and I think we probably took it further than most. But was it unique? No, I don't think so. I think most startup biotechs had to have some degree of that. If you started off trying to do things in a highly compartmentalized way, which is how pharma was then, and to a lesser degree is today, it probably wouldn't work.

Hughes: Yes. But it seems to me that it was sort of the same thing you were talking about in regard to American Hospital Supply, that there was freedom to make decisions and move in directions that you felt were necessary, and then probably Genentech was more the same and even more so?

Gower: More extreme, yes. It was more extreme because it had a whole different set of tools that opened up all sorts of possibilities in terms of drug discovery and drug development, which is after all the real business we're in. We put tons of labels on this business since I've been involved, and I've been involved since before biotechnology was coined. But the bottom line is, for 90 percent of the industry, it's about discovering novel drugs against diseases where hopefully you're doing something a little bit better or where there's not something at all. And that's really what this business is about. It's not about cloning things, which was

sort of a buzzword back then. It's not about the genome. It's about coming up with drugs, for God's sake. You use all those things as tools.

So one thing that Genentech had in spades over my experience with American Hospital was just lots of novel, new tools to get at some of these things, and so a lot more opportunities to go after drugs against disease that would be important, whatever that meant in various people's eyes. I used to kiddingly call it more toys to play with, which is the way I viewed it. I think that pushed the nature to which this organizational culture evolved at Genentech, that was much more so, even though I agree that the American Hospital thing was a good prep for this. In fact, it's probably no accident that the number of people from American Hospital, and even in fact that little tiny division, have ended up in biotech that have ended up in it. Gary Lyons, who's now president of Neurocrine, lots of people. Ken Andrews, who just took a job on the East Coast with Alkermes as chief business officer, Kim Popovits at Genomic Health. All of us started off in the seventies back at the American Critical Care division at American Hospital Supply.

In part, the atmospheres are very similar, but Genentech took it to another whole level. It had the tools to make many more possibilities available, so that you had to stretch yourself outside of whatever the theoretical boundaries were, because it was all new to all of us. So we all needed to sort of truly collaborate on these decisions.

And the other thing was that the expectations of Swanson—and because of him, the world—on what we could accomplish with it was so much greater, that you ended up having a much greater constituency inside of the company than I'd ever experienced for whatever decision it was you made or in theory were responsible for. I'd never had scientists, or even research assistants, come in and debate with me on how to price drugs. I mean, that was a novel experience. And a good one. Also, I remember very clearly my first year on the job going in to a scientific committee meeting on new programs that we had just started up. I was really out of my depth at that point. I knew medicine pretty well, but I had not fully nailed down this whole molecular biology, recombinant DNA thing, and much less did I know the codons that made up the common promoters and constructs to express genes, et cetera. So I was just trying to keep my head above water in this meeting, delighted that I'd been invited, when Art Levinson said to one of the guys who was there, who later went on to Amgen, as a matter of fact: "Well, that's all interesting, and yeah, we don't really know, but we can go this way, we can go this way, we can go this way, all of which makes some sense, and we may have to try all three to see if this works. But what I want to know is, at the end of the day if we do this, will anybody care? Jim, what's the market for this?" [laughter] I remember thinking about it, and I fumbled my way through something, because it was hard enough to figure out what the disease was, much less what the market was for a product that we hadn't even invented yet.

But I remember Art asked me the question—it certainly made an impression on me, maybe not as much on him—and I also remember saying to him later that that was the first time at that point in my career, of slightly over a decade in the pharmaceutical industry, that anybody in a research role in a pharmaceutical company had ever asked me that question. And it may seem obvious, [laughs] that researchers want to find something that is not just interesting scientifically but also useful, and make money on it. But it wasn't obvious. It was the very first time that that had ever come up. And that was just the beginning of things to come, where us business types would debate science with the scientists, and the scientists would debate business with the business types. That was just part of the way it was. It was a lot of fun.

Hughes: Yes, I can imagine. And Art probably spanned those two worlds.

Gower: Better than anyone. Art's a marvelous guy. I remember walking into his office in the early eighties after—well, let me back up a tiny bit. When I first got to Genentech, there was some sort of industry affiliate program down at Stanford—that Paul Berg was loosely affiliated with—that Bob Swanson had signed up Genentech for, for some reason—

Hughes: Oh, I know about that program. Yes, the biochemistry department had an industrial affiliates program—that's what it was.

Gower: That's it. And they were holding, I don't know, a two- or three-day meeting on biotechnology for the industrial affiliates. I remember going down, and I remember listening to Paul Berg talk about *Drosophila*, about *Drosophila* genomics. Now, I knew what *Drosophila* were, since I'd had a genetics class in college and I had to count those little suckers. [laughter] And frankly, those experiments hit me a heck of a lot like some of the engineering experiments I didn't like: I know the answer before I even do this, so this is just a test to see if I can replicate it. This doesn't teach me much.

But I remember, although I thought that some of the sessions were interesting, they weren't highly practical to what I was trying to get done at Genentech. So I went to Dave Goeddel and I went to Art and said, "You guys have got to help, I mean, this is useless for me. Give me something—texts, journal articles you think are useful, something I can sink my teeth into, and I can follow up and ask questions of you guys, so I can get up to speed faster, because I know part of this stuff but I don't know this part of it."

Art said, "If it's written, it's out of date." [laughter] Art said, "Tell you what. Just come by here tonight when you're finished"—I was just down the hall. "When you're finished over there, come by here and we'll just start talking." I remember his office at the time as being unique, because it was always messy, and his office still is, at least the last time I was in it. And he would have tons of

scientific papers on one side and tons of *Wall Street Journals* on the other. And I—

[End Tape 1, Side A] ##
[Begin Tape 1, Side B]

Gower: And he's not doing it because he's trying to groom himself to be CEO; he's doing it because he thinks it's interesting and it's the way he thought. And it's the way Goeddel thought, too. Only difference between the two is that Art would actually take the time to try to teach me something; Dave doesn't have the patience. Unless you could ask the question about four layers deep, Dave just can't deal with it. He means well, but he can't. But Art had the aptitude and the patience to deal with it from sort of the struggling basic levels, and it helped me get up the learning curve.

I remember that so vividly because it, A, was what I was looking for, not the industrial affiliates program at Stanford, which was just—let's throw some stuff at these guys and see what they can absorb. It was much more attuned to what I needed to know at Genentech. And B, it was just Art and the way his mind worked. He would flip back and forth between the science and the business constantly, and that was Art.

Hughes: Once you did get a better handle on the science, how did that interact with what I imagine your job really was, which was the marketing aspect of it, right? You had to know about the science, but that wasn't where you were going to be operating. You were going to be taking it the next step—

Gower: Right.

Hughes: Talk to me about that. Okay, you've got a promising research result. And then does it land in your lap? "All right, tell us if we should continue putting money into this project, because it has marketing potential?"

Gower: At that stage, various of us that were not on the science side, but typically myself, Bob Byrnes for the time he was there, although we really only overlapped for a year—

Hughes: Is that so?

Gower: Yes, he was gone in '82, I think. —Kiley or whomever on patents, Dave Martin in medicine. We were all involved, back to what I said Swanson's philosophy was sort of at the early stages: not trying to dictate where the science should go; the scientists should figure out what's possible first. But it usually turned out that we would have, for every idea we could possibly afford to do, fifty candidates. So it was more a matter of trying to get together and share thoughts that were a mixture of commercial and patent and financial, et cetera, in terms

of, well, of all of these, what's the best combination of the things that we think are scientifically possible, and actually likely to—more or less, if it works—have an impact in a clinical setting? And that at the end of the day actually can be a product that someone cares about. So we'd all be involved with it; yes, myself included.

At the end of the process of picking those commercial targets, and I'm really shortening that, but it's just as well for this, I had two primary roles myself. One, and this was especially true in the early days, and later it reported to me, was even before the marketing, the business development part of going out and doing collaboration deals so that we could pay for this stuff. In some cases, those were the collaborations with the [Eli] Lillys of the world, on human insulin, although I didn't do that one—that was before I got there. But more often than not, and in fact part of the whole reason I was brought in, was, "We want to do this more and more for ourselves, so let's find some ways to do some collaborations, but keep the North American rights for ourselves and build our own effort."

So a lot of my focus was: we have to build some co-development partners, so let's go find someone in Europe that's a medium-sized pharmaceutical company—which we could find at the time; it's harder these days—go find another partner in Japan, and then co-develop this thing with them and put it on the market in the U.S. It's sort of a combination of raising the money to get this done, which isn't all done on the stock market if you do it right, and later, the marketing of it—although we didn't get to that until 1985 when human growth hormone was introduced, halfway through the time I was there. I knew it would take that long, but—

Hughes: You did know it would take that long?

Gower: Yes, within about a year or so. We had one sort of slow-up with an advisory panel that cost us about a year in getting—That's the usual thing with the FDA: "This looks great, go back and get more data." So there was some thought we could get it on the market, say, a year earlier than we did, but there was not any thought of getting it on before that. So '84, '85, yes. And it ended up being October of '85.

Hughes: You're talking about human growth hormone now, right?

Gower: Yes.

Hughes: Except for the insulin, where was the pattern?

Gower: There was no pattern. And insulin and growth hormone were both approved in lightning speeds for the FDA.

Hughes: Why was that?

Gower: Well, two factors. One was they were known entities as drugs, being replacement hormones for the body in cases where either diabetics or hypopituitary dwarfs had a known deficiency, and you were simply replacing what was there. The other products on the market were in essence either animal-derived or actually purified in the case of growth hormone from human cadaver versions of the same thing. So this was a technology that would enable you to make it in much more plentiful supply, a lot faster, without impurities, so on and so forth, of a known hormone. That speeded things up.

Hughes: And a human one.

Gower: And human, yes. And that speeded things up tremendously.

And I would also say, the sort of growing recognition in Washington of the potential importance of biotechnology probably did help. It actually cut both ways, because there were people afraid of this unknown new technology, but at least when it got to the FDA, there was basically the opinion that at the end of the day, it would be a good thing if we approved these; let's just make sure these guys, since they're all new to the business, haven't somehow screwed this up in some way that's going to be dangerous. They actually were trying to help in providing a little bit more information than I had seen before, or have learned subsequently you always get, "Well, why don't you do the study this way"? And that probably helped the speed of it, for the first few approvals, I would guess.

Hughes: Did the science and the process throw the FDA at all? I mean, I would think there would have been a steep learning curve for the FDA itself.

Gower: It did to a significant degree, but I think this was also the period in which the FDA recognized this was coming down the pike, and it was a period where they used this fact to recruit a lot of folk from the NIH campuses to help them with that. The early drugs were all bacterial fermentation in *E. coli*. When you get right down to it, the process guys at biologics were used to handling antibiotics normally secreted from *Streptomyces*, versus the hormones secreted from *E. coli* made by Genentech; it's not that different in terms of the things you look at from a process standpoint.

But when we got to t-PA [tissue plasminogen activator], and then Amgen got to EPO [Epogen], you were dealing with a whole new breed of cat. It was the first time continuous mammalian cell substrates, read in some people's lexicon, "artificially engineered cancer cells," were used as a production vehicle for a human pharmaceutical. Because these were much more complicated molecules, and nobody had seen them in humans before, the clinicals had to be more involved. Unlike insulin and growth hormone. These were not—

Hughes: Because the molecules were tailored—

Gower: No, they were human molecules. t-PA is present in the body, as is EPO, but no one had ever had them in large enough quantities from anywhere to be able to use on super-normal levels to see if there could be a therapeutic effect. In the case of EPO, to stimulate the production of red blood cells; in the case of t-PA, to lyse blood clots at a much more rapid manner than the body could take care of them themselves—if that was for instance causing a heart attack, that was our first indication. So there was new clinical information to be gotten, but also the process, which was your question, was much scarier, because you weren't dealing with something that the agency had a history of experience with. Drugs being purified from bacterial cultures: they had that. But drugs being purified from mammalian cells that have been engineered to be immortal and have who knows what oncogenes in them, and all sorts of things that you can always imagine would be an issue, that was new. So we actually—

Hughes: And how did Genentech get around that?

Gower: We engineered, through a lot of hard work of a lot of people—Dave Martin, Art was involved, Jack Obijeski had joined us from the CDC—who was head of molecular virology at CDC and was working on the vaccine programs at the time—basically orchestrated a consensus conference among the NIH, FDA, World Health Organization, some of the vaccine groups around the world (it clearly applied to vaccines as well as therapeutics) on the issue of using continuous mammalian cell substrates. This included determining what should be the criteria for both checking the process and checking the safety of the ultimate product and deciding if you should test for oncogenes specifically.

At the end of that process, it made a lot of folk more comfortable, and certainly on the part of the FDA, that we did have something like a supra-advisory panel, but with many more people involved, open to the public, and with a lot of really heavy-duty luminaries in the field. And we had sort of a consensus statement of why we need these things, because you can't make these kinds of drugs in *E. coli*, and here's what we ought to do to make sure that they're safe.

And one of those things, to answer your question—Levinson had a lot to do with this, since several of his early papers when he was in Mike Bishop's lab on oncogenesis—was we put together something that was fairly unheard of at the time, which was we actually made probes and probed the final molecular soup and the purified protein product for known oncogenes. That was a release criterion. Now, for the mid-eighties, that was out there.

Hughes: I can imagine.

Gower: And also, to be perfectly frank, we saw it as a competitor hurdle, because we didn't think a lot of our competitors could do that.

Hughes: Yes. And it was true, wasn't it, for a time?

Gower: True. It did create a hurdle that was quite hard.

Hughes: With the FDA.

Gower: Yes. But it was also a tangible way to address the potential safety issues, although you'd be hard-pressed to find any of the scientists at that point who really thought that you couldn't purify the oncogenes out, for instance. But you don't know what you don't know, so the fact that we had put together a process that enabled people to say, "Well, if you could do these things, that would be a pretty good sign that it was safe." It has turned out that that is safe, and indeed, I don't know the ratio these days between bacterial fermentation and mammalian cell culture for production of recombinant DNA products, but I would certainly say it's well tilted towards mammalian cell culture these days for most everything that's come out, and there's good reason for it. So it worked out, but it was an issue at the time, yes.

Hughes: I've read that one of Genentech's strengths was the variety of [protein] expression systems that it had.

Gower: That's true.

Hughes: And not only had, but beat others to it, right? I mean, what was there other than *E. coli*, yeast, and mammalian cells?

Gower: Well, there were a number of other experimental approaches. The ones that we focused on were those three, but you've got to keep in mind that at the time that we were focusing on all three, most other groups were going only with one. And virtually none of those included CHO [Chinese hamster ovary] cells, which turned out to be the most valuable of all. Chiron, for instance, was built pretty much on a platform of yeast.

Hughes: Right, with the hepatitis B.

Gower: And we did hepatitis B in both yeast and mammalian cells; for various reasons you couldn't express it with *coli*. We did lots of things in *coli* as long as it worked, but the fact that we had not just the scientific capability but probably more importantly—and this is, I think, one of the things that was not well appreciated certainly during the eighties and to some extent to this day in terms of the edge Genentech had—was the incredible process scaling capabilities in working with these things that Bill Young's group ended up building. It's very different working with *coli*, yeast, or CHO cells in the lab than it is working with a 1,000-liter fermenter. It's just very different. You end up having to go back and redo the science yet again just to get it to work at a commercial scale. I think that that was a huge edge for Genentech during the eighties and early nineties, so I'm amazed people didn't catch up quicker than they did, but they didn't.

So working with multiple expression systems, not just in concept, but at the stage where you could produce GMP product [Good Manufacturing Processes, required for FDA-approved drugs] the FDA to me was a huge differentiating factor. If I could put a slight twist on what you said: lots of people can work with these things in the lab. It's a whole different thing to take them to the FDA.

Hughes: My impression of Genentech in comparison to Cetus is that Genentech would put time and effort into developing these new systems, but it was always with a marketing goal. This was not just a research project in the way that I have had the feeling that it was at Cetus. I'm not expressing myself very well—

Gower: No, I got it.

Hughes: But a very goal-oriented form of what could be looked at as fairly basic research. Can you produce drugs in a mammalian system and—

Gower: We're doing this because it differentiates the company, as opposed to we're doing this because we've got a goal in mind scientifically—yes, I understand.

Hughes: Yes.

Gower: See, I view all of them as marketing goals, but then I would since I come from that background. I mean, I think it all depends on what your goals are. If you're trying to impress Wall Street, to this day, you can come up with a scientific concept that you focus on and say that that differentiates you as a company. Luckily, at Genentech, our focus was a little bit longer term, which was: what will it take to get to the products? Swanson made sure it stayed there. So I would differ or rephrase what you said only slightly, in that I think there was a clear business goal, but the business goal was focused on what is going to be the expression system required, and the best system to come up with to produce our product? It was not just a differentiating feature that we can talk to some biotech analyst about and say, "Well, we can do this in *Pichia*," [a yeast species] or whatever.

In fact, I remember getting a call from some analyst in the eighties who said that since we had the capabilities of producing things in yeast, why were we doing our hepatitis program in the clearly more expensive, and therefore by implication less useful, CHO system? And I said, "Well, it's because we actually bothered to do the work, to do it in both, because we weren't sure, and we found that you get a better product out of the CHO system." Actually, that's work Art did. And was it at the end of the day the biggest thing in the world? No, but at the end of the day, Merck licensed the Chiron product, Recombivax—but SmithKline licensed the Genentech product for Europe, and Mitsubishi and many others licensed the Genentech product for Asia. Merck ended up having to take the license even under yeast for Genentech, because we had done that work, to take it all forward together. Really it was Art's call, together with the MDs—

the sugars are slightly different on the CHO cell-produced material, and we actually took it into animals to see which was more antigenic.

So, believe me, it was marketing-oriented as well as science-oriented. You wouldn't do those studies if it was just to say it to Wall Street. But our goal was to try to come up with the best product. Now, you can always be wrong, but at least we tried, and that was the real goal of those expression systems: to have the ability to move between expression systems and to pick the best one for whichever products we're going at. So I don't know—is that a science goal or is that a business goal? Hard for me to say. I mean, it's both. And again, the crystal-clear goal that Bob set in place for everybody was: Our aim is to put products on the market.

Hughes: And that was his mantra?

Gower: And everything flowed from that. There were others that were crystal clear on that too. George Rathmann is another absolutely crisp example. But without naming names, there were times when I couldn't quite tell what the goal was, of some of the other groups.

Hughes: You mean some of the groups in other companies?

Gower: Yes. Was it to appeal to Wall Street short-term with their scientific prowess? Was it to be so "marketing-oriented" that you weren't willing to listen to what the science tells you, in terms of what the outcome was? I can't guarantee it; it would be better to have the science guys interviewed at Genentech on this. But I'd like to think we kind of thought about both at the same time. I assure you there was no reason for Art to do two expression programs at the same time, in the same lab, if we weren't trying to come up with the best product in system for hepatitis. We weren't intellectually trying to prove that we could do it in yeast and CHO cells at the same time just to say, "Hey, look at us, we can do two at the same time that other people are doing one." That doesn't get you anywhere.

Hughes: Did the scientists in general buy into the fact that what they were doing, which was really for a different goal than what any of the academics had been doing at universities, to have the market always as their ultimate end point, rather than discovering basic science principles?

Gower: Most all of them did, and there were a few exceptions of really excellent scientists, some of whom were good friends of mine, who didn't quite track with it the same way. Over time, some of them stayed, did useful things, but most of them ended up leaving. I probably couldn't phrase it any better than Goeddel did way back when, and he used to be very forceful with the scientists: "In this industry," he would say, "You can do fabulous science, and you have the unique ability to be in *Nature* with your results and in the market with a product at the same time. We want to do both." There is no reason, beyond philosophy, of

differentiating between academically excellent science and that's commercially viable. They are not incompatible. When you get to a mature industry, maybe they are; I don't know. I've never been in one. But certainly not then, and I would say still not now in biotech. That's one of the real beauties of it, which is that you can do true cutting-edge research, and yet still be focused on commercial goals. At least in the health care part of it. A little tougher in some of the other parts.

But that was certainly both Art's and Dave's philosophy. Those were the two folks that most people looked up to. You had the Axel Ullrichs of the world who did brilliant science, but he had a hard time focusing beyond the paper that would appear in *Nature*. So we just didn't use him that way. But even he didn't have a hard time tuning into the fact that the two were compatible goals. Its just that he was unlikely to be the one you would want to put on a tough expression problem or tough cloning problem, towards something that you felt was a commercially necessary thing for Genentech. That always revolved around the same two guys in the eighties: you wanted Dave to clone it and you wanted Art to express it.

Hughes: [laughs] Yes. And I think also, you can turn to Genentech's spectacular publication record in those early days as confirmation of what you're talking about.

Gower: Exactly. And that was one of the big discussions we had in the early eighties, and Tom Kiley was a bit involved, because obviously it implied some things you had to do on the patent side so that you had the ability not to impede the science and the publications. And we did do that. Tom recognized the benefit just as I did. But there were none of us that had a question of whether a commercial entity should allow scientists to publish this stuff. That wasn't an issue at all. The issue was how do we work it out so that we can do both, and not hurt ourselves in the patent office.

Hughes: And had that system been worked out? When and how Kiley would come in to that movement from science to publication, by the time you arrived in 1980?

Gower: No, but it was evolving. It had been thought about; it had been discussed, and it had been certainly started. I would say during the entire period of the early eighties, and I don't know how to put a date on it, but certainly '83, '84, up to then, we were continually refining our approach to publicizing and patents. We had constant discussions on that until everybody finally said, "Well, this works pretty well; we're close now." It may not be perfect, it never will be, but we've got most of it worked out.

Hughes: And was it around what goes into a paper and what doesn't go into a paper? Was it that kind of level discussion?

Gower: Rarely. The only thing I can remember in terms of a discovery that specifically would go into a paper was the DNA sequence of gamma interferon. At the time, everyone thought that gamma interferon was going to be the ultimate drug. It's going to cure cancer, viral disease. Of course, anything that appears on the cover of *Time* magazine as "a cure" is almost inevitably doomed for failure. But certainly a lot of people bought into it; it wasn't just us. It was most of the industry, most of academia. So when at the then annual interferon meeting, in San Francisco, Dave Goeddel presented the cloning of it, there was a lot of discussion on putting the sequence in. The fear was that others would just go copy the work. So we debated that whole thing yet again. When you said, "Was the publication policy in place?" The beginnings of it were, but we continually evolved it over specifics, a set of examples. Practically, the question was always when, not if.

Hughes: And did you, in that case?

Gower: We did end up doing it. There were some that were for and there were some that were against. Interestingly enough, it wasn't all the scientists were for and all the business guys were against. It wasn't that way at all. And we did decide to do it. I remember standing there in the meeting; when Dave put that slide on the screen, it was like a forest of crickets erupted behind me, with all the motor drives on cameras that were taking pictures of the slide with the DNA sequence.

[End Tape 1, Side B] ##
[Begin Tape 2, Side A]

Gower: Here's the holy grail, the secrets of gamma interferon. And it actually wasn't that hard a decision to come to. I think it probably was just the fact that it was the biggest test of what we had decided.

Hughes: And why had you decided to publish it?

Gower: Oh, I'm sure you'll get different answers for that from different people; I know the best answer would be from Dave, who was closest to it. My catch was that the sequence of these things—much as I would come to believe over a decade later about whole human gene sequences—were a necessary tool to start with, but were far from being a drug: The output of this technology was not a sequence for a specific cytokine; the output was a drug. And in the case of gamma IFN, it didn't quite work out that way. It did get approval for chronic granulomatous illness disease, but it certainly did not revolutionize the treatment of cancer or infectious disease.

Hughes: Am I understanding you correctly, your argument was that putting up the sequence was a long way away from having a marketable drug, so why not put it up?

Gower: Correct. If it gets the recognition for the science that Dave did, if it helps us recruit and attract better people because they can publish, if it helps us get the attention of the medical community and encourages them to want to work with us, we'll have an easier time doing the clinical trials. All those things are intangible benefits that far overweighed, to me, the temporal competitive advantage we might have by having the sequence to ourselves for, what, a few months? A year? There were other good groups out there working on it, it wouldn't have taken that long. It's a long race in the pharmaceutical business. It's getting longer all the time. Around ten years, these days.

So I was pretty comfortable, as I believe Tom Kiley was, in saying, "Well, I think we need to have the patent filed, because if we don't, somebody else will file it." But I didn't even see that as being the key thing. The key thing is to turn it into a product.

Hughes: I think of decision-making in the pharmaceutical industry as being much more compartmentalized. The scientists do their science; then the development people come in or whomever—I'm not even sure what the sequence is. But these groups aren't putting their heads together and having a real discussion about where it is with the science, where it is with the development opportunities, and where it is with the marketing potential. It moves in a very regulated way, without too much interaction between these groups.

Gower: The groups decided this together.

Hughes: Yes.

Gower: I think that it is one of the distinguishing characteristics of Genentech, and it all started from Bob Swanson, because that is the way he wanted to think about things. It wasn't required that he necessarily be in on these discussions. Now, he was in on most of them, but not all. He was very comfortable with hiring people that he thought—whether true or not—were smarter than he was. That's what he always used to say. He would really look for, on most things, if those of us in disparate areas have our act together in terms of: have we thought about this, have we talked about this, were we coming at it from more or less the same place in terms of the answer? Whether we got at it different ways or not, that's just human. You wouldn't have a hard time convincing Bob to do something that he thought was 180 degrees away from his first catch on it, if the key areas came to that decision together. And that was a rare quality. There's actually a couple of layers to that. Bob encouraged that thinking, and he made it true for himself as well.

Hughes: But in the end, somebody, or maybe somebodies, has to make a decision.

Gower: Sure.

Hughes: And is that decision-maker going to vary from situation to situation?

Gower: Yes. Sure. I think there are least a couple of models of that. On the one hand, if it was something that involved purely in deciding scientific issues, you're going to let a scientist make that decision. What am I going to add to that?

Likewise, and we did get to a couple of these, if it was thrown to Bill Young's group and it's a matter of yes, but we can't scale it up. [laughs] You may think that that's scientifically the best system, but we can't scale it up.

Hughes: You *can't* scale it up, or, we don't have the resources, the time, the money, the whatever to work out a system to scale it up?

Gower: Either. And sometimes it was both. Sometimes it was a question that we really don't know how to get from here to there. Therefore, if another approach is only slightly less ideal from a scientific standpoint—and the marketing guys don't care at all—why don't you do it this way, because this we do know how to scale up to a level that we can produce GMP—good manufacturing-based process—that will produce material that we can put in clinical trials. And that didn't happen a heck of a lot. But at the end of the day, if it came down to something that someone in a specific area had to do, people were pretty good about backing off and letting them make a decision. Likewise, there were things that came up—a lot in the clinic. The design of clinical trials is as much an art form as it is a science. It's really difficult. But you have to hire people that you trust to make those decisions. We would all argue about specifics, but rarely did it actually ever get to a point where someone would say, "Yeah, but I can't do it that way, I can only do it this way." But if it did, you go with the guy that's got to run the trial.

And ultimately, when you get to the marketing, same thing. The only time I can think of where that would be the case in the marketing was the pricing. For the most part, the rest of the stuff was pretty easy on my folk. But pricing was always touchy, because we were always worried in the early days about pricing it too high or pricing it too low.

Hughes: Well, how did you even begin to think about it? Particularly with drugs that had no exact counterpart?

Gower: It's always been the most difficult thing in the pharmaceutical business—again, this transcends biotech—for a completely novel therapeutic, to figure out the market. And it applies both to the market size and the price. And the market size for drugs heavily influences the latitude you have in pricing.

Hughes: Is that so?

Gower: Sure. You know how much you are likely to spend on it. You look at the market for a novel product by forecasting patients who will use the drug in circumstances where nothing is used currently. Then you estimate the price range that will generate enough return to pay for the existing costs and provide funding for new research.

For something brand new, and a good example of that from a non-Genentech product would have been Merck's hepatitis B vaccine. It is a tough call. I've talked to the Merck guys on a number of occasions over the years about the similarities between the hepatitis B vaccine and t-PA: Nothing like this had existed before, and you've got pressures on both sides, because you have investors that are counting on this to be a *huge* deal, and you've got people that are counting on it to be affordable for patients.

Hughes: Yes, exactly, that's the catch-22.

Gower: You've got a tremendously expensive program, but there's nothing out there to guide you in terms of how many people are going to get treated. Merck over-forecast the market for hepatitis B, both for the original Hepavax and the eventual Recombivax, by two to three times, because it seemed obvious to them—and I would agree with them—that at least health care professionals would get vaccinated. And yet, I remember very clearly in the early eighties when there was just Hepavax, that there was a study at Duke where they had mandated the use of the vaccine in high-risk health care professionals, and only 10 percent of them percent used it. So it's a tough call, but you're always trying to hedge your bets and pick a price that at least will cover the cost of development, and ideally it will cover the cost of development and the future things you've got in research.

Hughes: And, what about all the research that didn't lead to a product?

Gower: Well, that gets into the more complex argument regarding the cost of drugs, and I really wasn't going there. If you're going to stay in business over the long haul, you have to include the cost of research and the cost of capital in drug pricing. It isn't always a factor that you take into consideration for the pricing of any individual drug. But in terms of the individual pricing for a specific drug, you've got to at least make enough to pay for what it cost you to get from here to there, and contribute enough to the general return for investors so that you can keep the business going. Ideally you try to price in a way that does not cause too much of a problem in terms of the expense of the therapy for the population it's intended to treat. These days you almost can't win. It's a lot tougher now than it was back in the mid-eighties, and I thought it was tough then. There's no right answer. Unless it's free.

Hughes: [laughs] Talk in this respect about t-PA, because that is what immediately leaps to my mind when you talk about pricing differentials. Roughly speaking, my

memory is that it was something like $2,000 a shot for t-PA, as opposed to streptokinase, which was $200.

Gower: Correct, yes. $2,200 versus $200.

Hughes: And yet that GUSTO trial, and again I can't remember the figures, but the difference in efficacy was not that great.

Gower: No, it wasn't, not based on mortality. However, it was statistically significantly different, and in favor of t-PA, but—

Hughes: Can you use that as an example, though, of how you—

Gower: Yes and no, because we had to set the price several years before that. GUSTO didn't come out [until] the early nineties. There was one study that had been done, which had been done in Italy—over our objections with our European marketing partner—which compared a slightly different regimen of t-PA, of which I won't bore you with the details, but it was a matter of how it included heparin in the protocol. And basically showed statistically that there was no difference between streptokinase and t-PA in terms of mortality. Now, that study got redone in a much bigger study between U.S. and European centers using heparin the right way, which led to the result you're talking about [in the GUSTO trial]. But at the time we actually priced it, we were facing a fact that the only study showed no statistical significance in terms of the difference between the two in mortality.

So, what do you do? Well, what we did is talked about it a lot. We also did every type of market research-type of study known to man, including some fairly sophisticated quantitative analysis, among physicians. Come up with a price that would at least pay for the development of t-PA, which at that time was the most expensive thing that we had done at Genentech by a long shot. Those trials were huge, compared to growth hormone. But even with a high price it wasn't big enough. Which is an interesting statement in and of itself.

Hughes: Yes.

Gower: It was $200 million in the first year. But we were wrong about the total number of patients that we would be able to access in the coronary care unit, within the first six hours after the onset of chest pain symptoms. We tried to estimate the number as precisely as we could; we even did a lot of joint work on estimating the patient population with American Heart Association. But you can never address precisely the subjective things, like ER physicians' reluctance to ship the patients upstairs to the CCU incorporated until after the drug is marketed

Hughes: You mean they want to hold onto them?

Gower: And it wasn't a malevolence; it was both habit and "what's in it for me." The entire history up until that point had been, rule out MI [myocardial infarction] based on somebody presenting with chest pain. They would do a chest x-ray; they would do an ECG [electrocardiogram]; and they would pull blood for cardiac enzymes. The enzyme results often would not return for another three hours. So they let the patient sit there. The reason is that before thrombolytics and coronary angioplasty and stents, there was nothing they could do anyway. They were basically dealing with treating the symptoms that came with the heart attack. They did not consider trying to intervene in the MI process itself. So there were decades of history of treating patients on a rule-out basis.

The cardiologists understood that things had changed, but the ER guys didn't necessarily. The additional factor was possible side effects with thrombolytic therapy. And, the side effects people worried about were strokes, because a thrombolytic can't tell a good clot from a bad clot. You can try to avoid high-risk patients, but that's a fact. Thankfully the percentage of patients having a stroke on thrombolytic therapy is offset by the percentage that survive who otherwise would not. The FDA even took note of the odds ratio for this as part of their approval decision. The balance is overwhelmingly in favor of treating the patients, but it's a tangible risk.

So you have the ER guy who can only see the downside of the therapy, who doesn't have a prayer of seeing the upside. The cardiologist is going to observe the benefit. So human nature is working against you, too. Because of this risk, the market did not evolve anywhere near as rapidly as we forecast. So, we had assumed that by pricing at $2,200 a dose, we would, within a period of two and a half to three years, cover the overall cost of all the development, and add enough to cover the other research stuff going forward. Because we undershot the market forecast, I could actually make the argument that in retrospect, if anything, I should have priced it at twice what I did.

Hughes: [laughs]

Gower: We were going to get the same amount of heat anyway. And in this day and age of Avastin costing $147,000 a year, it doesn't look so bad, $2,200. But that's now, and then was then. At the time, we thought we were being pretty aggressive. I remember talking about it, and we thought that $2,200 was as high as we could take it. The only objective measure we had was, if the patients got angioplasty, what would that cost? And the answer was $9,000.

Hughes: But why wasn't streptokinase out there? I mean, maybe the GUSTO trial was a few years off, but wasn't streptokinase being used?

Gower: No, it actually wasn't. People were afraid of streptokinase because it caused such generalized bleeding as well as stroke. The amount of streptokinase used in this country was tiny. Even in Europe, the amount being used in the centers in

Europe which had pioneered that type of therapy was fairly small, because the bleeding issues caused concern.

Hughes: Yes, it doesn't sound it.

Gower: I said at the time that what I didn't understand was why more patients weren't being treated. I always used to say, "I show up at a local hospital, even if you've got to treat me with streptokinase, for god's sake, treat me with something!" I mean, don't do nothing. But that was what was happening in the U.S. And t-PA, in spite of the $2,200 price, basically penetrated the market that was penetrable early, almost overnight. That's one of the reasons for those early first-year sales. For the teaching centers, the centers that were geared towards having cardiologist on staff twenty-four hours a day, it had almost immediate uptake of thrombolytic usage, an immediate paradigm shift. That was in 20 percent of the centers in the U.S., and it took years to get beyond that percentage. Now it is part of the routine standard of care. The pricing of t-PA did not impede our ability to penetrate the market. What I did was—it was ultimately my responsibility. There were a lot of verbal outcries at the time of, "How can you charge ten times as much as streptokinase"? But it didn't stop anybody from using it. We all talked about it back then; we all talked about the fact that no matter what we price it at, it's going to be perceived as too much—unless it's $300 or less.

Hughes: But then when GUSTO did come along, or the results therefrom, wouldn't that have provided a huge argument against t-PA, in that here you've got a very expensive drug, and you've got a ten times less expensive drug that seems to work almost as well?

Gower: Actually, it was just the opposite. T-PA was pretty much established in the marketplace before GUSTO came out. But the strong results for t-PA in GUSTO basically converted all the remaining systems that were not using the drug. A good example is Kaiser here in the Bay Area, where they were basically saying, "Until there's absolute proof, we won't let you, the cardiologist, use this. You can only use it in very specific patients." They would set up these restrictive criteria trying to limit its use, whereas if you showed up at UCSF or Stanford, the patients were all getting treated with tPA. When the GUSTO trial came out, even the HMOs said, "Forget it, just use t-PA." The GUSTO results showed t-PA saving more lives.

Statistically there was a significant difference between mortality on t-PA and streptokinase, but it's a small percentage of difference. Less than 10 percent of the patients in the U.S. die of a heart attack. But how do you equate that with the fact that the other studies have shown that despite that, over twice as many patients on t-PA had their heart muscle either saved entirely or more of it saved? Well, that was true, that data was available in the trials, but it wasn't part of the actual approval. It depends on how you value something in this area of medicine. The practical point of it is, to this day, most physicians in the U.S. use

t-PA. I don't think it's a very hard decision. But the controversy at the time gets back to that highly statistical regulatory-approval argument. Well, is that worth it at $4,000? I don't know. I mean, it all depends on the perspective of who's making the judgment. But it's certainly not necessarily a rational argument to say, "Well, Aresta makes 10 percent greater live; the standard therapy before that as third-line therapy made 8 percent live. Because that's off patent, that's only a few hundred dollars versus a few thousand, therefore I'll choose the one with a few hundred because it's a more rational economic decision". It's fine with me, as long as it's not me or my family.

Hughes: Yes. [laughter]

Gower: But I've been in this industry too long. I will always go for that [drug] that there's the best data on. And that was sort of the situation with t-PA. I don't know if that answers it, but—

Hughes: I think it does.

[End Tape 2, Side A] ##
[Begin Tape 2, Side B]

Hughes: I hadn't before heard the pricing dilemma in such detail.

Gower: Well, it's an interesting problem. I mean, we're going to face it more, and in some quarters this issue is getting to a fever pitch these days. There are very strongly held beliefs on what we can afford as a health care system, and where new drugs fit in, and for that matter where do new therapies fit in period.

Hughes: To say nothing of the problem of drugs in developing countries, as we're witnessing with the AIDS drugs.

Gower: Who can't afford any of the above.

Hughes: Yes, exactly.

Gower: That's another whole interesting question. I think I'll opt not to tell you the story about a visit I paid to the WHO [World Health Organization] once on hepatitis vaccine. [pause]

Hughes: Tell it, if it's relevant.

Gower: It's not, to this. It's just that I admire Merck and Pfizer for the way that they go at the problem, and at least they do the right things from a politically correct standpoint and a public relations standpoint. But the problem is almost unsolvable, and it's certainly not by drug companies or individual countries alone. Those people need a health care system; they don't just need AIDS drugs.

I mean, that's the problem. And I don't think you'll find many of the big pharmas that wouldn't just donate the HIV drugs if they thought they wouldn't float back and go into the markets here, and if they would get used over there. But it's a much bigger problem, it's a huge problem there. It's not easy to figure out.

The reason I mentioned Merck: Merck has for years given away Ivermectin, which was originally designed as an animal drug, but is useful in humans for parasitic infections. It treats river blindness—it's wonderful. And they give it away. Most of it goes out of date sitting on the docks wherever, because you can't get it to the people in the [hinterland].

Hughes: Well, and also, Merck is Merck. Isn't it one of the largest pharmaceutical companies, and what is a small startup biotech firm do in these cases?

Gower: No, I think within reason, most of us would give away stuff too, and have. I mean, Genentech had compassionate-use programs. These weren't particularly Third World issues, but for both growth hormone and t-PA. The cost of manufacture of drugs has never been a big deal. Drugs are relatively cheap to manufacture; it's just that they cost hundreds of millions of dollars to develop and get on the market. So that's what people are paying for. They're not paying for the manufacturing cost. There's a fair amount of latitude to make compassionate-use programs and giveaway programs of various sorts feasible

But t-PA was a fun one. It was something that we thought about a long time. It was something that we probably over-researched, given the ability to ascertain quantitatively the subjective issues that were involved, because we were trying to do the right thing by it. At the end of the day, I probably would have done it a little bit differently, in a different direction, than I think would have been the one chosen by some outside observers, really. It certainly wouldn't have been to make it cheaper.

Hughes: The other thing, which I guess goes without saying, too, is that much or most of Genentech's eggs were in the t-PA basket.

Gower: *Precisely*, which is why I would have done what I just said. I felt guilty for a number of years, because if we could only have figured out a way to do better on t-PA, we would have had more wherewithal to take some of the stuff that Art ultimately got to push forward into the clinic sooner, better, faster. I'm very comfortable, in looking back on things, that we did just fine, but I still felt guilty about it, because it had a huge impact on the company. My feeling at the time, although it's not my feeling currently, is that it might have also made a difference in terms of selling the place to Roche [Hoffmann La Roche]. We had, at that point, our eggs resting in the t-PA basket; Amgen's eggs were resting in the EPO basket. I know from my own experience that we thought t-PA would be

somewhat bigger; George [Rathmann] didn't think EPO would be anywhere near as big as it was. [laughs] Such is the way life is.

Hughes: Yes, exactly. I know of at least two programs that were stopped or at least slowed—and I'm not saying that there's a direct correlation with t-PA—but this comes mainly from talking to certain scientists who were upset that the vaccine program were pretty much dead in the water after a certain period of time.

Gower: Sure. You mean the AIDS vaccine?

Hughes: Well, the AIDS vaccine, and I thought—

Gower: Because the other vaccines were dead before that. *Well* before that; it had nothing to do with t-PA.

Hughes: Yes. I'm trying to think of the—

Gower: Foot-and-mouth disease?

Hughes: Foot-and-mouth disease vaccine, yes.

Gower: Oh, you talked to Denny [Dennis] Kleid.

Hughes: Yes.

Gower: He's the only person on the planet that would mention that, as opposed to if you talked to [Jack] Obijeski or to Don Francis—who I love; Don Francis is the only chance in my entire life I had to actually work with somebody that's a real hero. I love that guy. But everybody else would mention HIV, but *only* Dennis would mention foot-and-mouth vaccine.

Hughes: Yes, it was Dennis. [laughs]

Gower: No one really cared about the commercial prospects for a foot-and-mouth vaccine. But that was well before t-PA. That had nothing—

Hughes: So nothing to do with that.

Gower: Zip.

Hughes: But were you involved in that decision?

Gower: Which decision?

Hughes: To cool the vaccine program. Or perhaps it wasn't so much that Genentech was shying away from vaccines for whatever reason, which could be liability, not

bringing in a big amount of money, or whatever else there would be; or was it specifically that the AIDS vaccine program was not getting where it needed to get fast enough? Was it AIDS, or was it vaccines that were being downplayed?

Gower: Both things were true, but to different degrees at different points in time. It was more complex than that. First of all, foot-and-mouth disease was gone well before t-PA hit the market.

Hughes: That was early eighties, wasn't it?

Gower: Yes. That was out-licensed to Bayer, because it's a non-U.S. market to start with. There is no foot-and-mouth disease at this point in the U.S. It's mostly a South American and, to a lesser extent, some European countries' problem, so you needed to have someone that would have presence in those markets for animal vaccines. By the time we got into 1983 or1984, we were firmly committed to human health, so that the whole animal health program didn't fit and it was sold. Foot-and-mouth disease went with it.

Then, of the vaccines that were remaining, there was hepatitis, which I was definitely involved with, because that was a human effort. I later ended up having the animal health effort report to me in the later part of my job at Genentech, but not in the early eighties; only after Bob [Swanson] had decided we ought to shut it down—thank you, Bob—[laughter] great, thanks a lot! The thought was, we'll be lucky to make it as a pharmaceutical company; we need to focus our efforts..

Hughes: And yet, there were companies out there that were doing just that.

Gower: Chiron.

Hughes: Chiron, Cetus, Amgen.

Gower: No, not Amgen. They were focused on human health by then too. We didn't believe in taking on an overly broad business strategy.

Hughes: Amgen in the very earliest days—

Gower: Chicken growth hormone, indigo dye, yes. But George just didn't have any other choices until he got to cytokines in '83 or so, which is when they started to focus their programs on EPO and GCSF. And of course, Applied Biosci, the science behind Applied Biosystems, was originally part animal too, but even at the venture studies that was pulled out and made a separate company.

So yes, you had Chiron working on diagnosis and vaccine. But I think that of the two strategies, Genentech's strategy worked better. Let's leave it at that.

Hughes: And you're saying that Chiron did decide to become a vaccine company and—

Gower: Vaccines, diagnostics, therapeutics—

Hughes: Three different companies—

Gower: Yes. And I think that's very hard to do. At the start of biotechnology, all these things looked doable by biotechnology. But as more of the companies got into the doing of them, most decided that—as Genentech did, and I think correctly—that you have to focus on something. It's very hard to be all things to all people as a startup.

Now, HIV I was involved in, because it was human health. The proponents of the HIV vaccine, which were certainly Phil Berman, Jack Obijeski, certainly Don Francis—that's why he came to Genentech. It was a constant push and pull for the entire time I was there. I think all of us felt that if this was doable, it was a good exception to our general rule of focusing on therapeutics. We weren't tremendously interested in going in and doing better measles, mumps, rubella—not because it wasn't scientifically possible, but because lots of things were scientifically possible that were much less risky and much more commercially viable—things that were just as scientifically important and just as medically important that we could focus on.

HIV was—it was its own thing.

Hughes: It's still its own thing.

Gower: Yes, it really is. It's certainly important if someone could come up with a vaccine for it. Recently, it's been through another life span, and that was the Genentech program, which became VaxGen, is now out of VaxGen, and Don and Phil are into a nonprofit foundation, and maybe it will work. I don't know. I hope it does. But the best I can answer your question on HIV, we were kind of afraid to stop doing research on it, because it looked good enough that it really just might work, and who would want to have made that call, or have that on their conscience?

Aside from HIV, none of us had much of an interest in vaccines per se, because they were and are the business they are. Vaccines are a difficult commercial business.

Hughes: Yes, I can understand. There's so much context just around AIDS vaccines that it immediately moves it into a different sphere.

Gower: And we actually discussed at one point combining our program with Merck's program. I was for that. At the very least, you would end up having another set of people with a whole different focus, who were also experienced in vaccines,

and if nothing else, we would share the cost on it, because no one knew if you could make money on this. You might have to give all of it away. Think about it from a commercial standpoint. But that didn't happen for some not-invented-here reasons here at Genentech, which I won't go into.

So vaccines: three different answers. Foot-and-mouth disease: no one really cared except Dennis Kleid, because it was his favorite. But it was a market that we shouldn't have been in. We weren't in animal health, and it's not in the U.S. HIV we did pursue, other human vaccines we did not.

Hughes: Well, you weren't after a time, but my understanding is that in that initial flush, it wasn't clear what kind of a company Genentech was going to be.

Gower: True. But by the time that we got to the point of our deal with Bayer on foot-and-mouth vaccine, it was crystal clear. That would have been about 1983

Hughes: Yes. We're over, but do you have time for just one more question?

Gower: Sure, I do.

Hughes: I think I know some of the answers, but to get it on tape: just to finish up this discussion, which has segued into why Genentech became a human pharmaceutical company—why did it? With these various avenues that in the beginning looked promising, when and why did it decide that human pharmaceuticals were going to be its focus?

Gower: In 1983, at the Silverado Resort, at our offsite yearly planning, for director level and higher, we picked human pharmaceuticals out of all the things that we were doing. Swanson originally, as with many of the original biotech companies, did see that all of these areas were promising for biotech. Initially, we did have some effort in all of the areas.

As we got into it, two things stood out. Number one, that the still-lingering public policy/public fear issues coming out of the Asilomar conference, which shut down recombinant DNA experimentation for a couple of years, '76-'78, were still with us in the early eighties, but to a much less degree. And one can draw parallels to the current time, the GMOs [genetically modified organisms]. People are always afraid of the unknown. For Genentech, we saw the risk-benefit equation as being clearly on the side of using recombinant DNA for curing people of diseases. I think that's about as much logic as was put into it, but it was true. And that's still with us to this day. Whether it's people wandering around in San Francisco dressed in butterfly costumes to protest GMOs, one would think they'd never read the follow-up to that lab study in Cornell in the field trials that the Environmental Protection Agency did that showed that actually for butterflies, more lives were spared by the use of the BT-modified corn—but, hey, a true believer can never let the facts get in the way.

But it's a hotter emotional issue. GMO organisms are bad, using growth hormone to make our cows produce more milk or something that—certainly Berkeley Farms, which is what I use, advertises on their label that that's something that they don't do.

And I think that in retrospect, that was a really good decision on our part that the area that this technology had the greatest public benefits versus risks was in human health, and that it was going to be easier for Genentech to succeed by applying our technology there. Number two, we had people that were out of academic programs that were mostly trained in the molecular biology of human health. This was a very natural thing. Axel Ullrich and Peter Seeburg had come out of Howard Goodman's lab at UCSF, involved in the cloning of the insulin receptor. Art had come out of work on oncogenes. Goeddel and his background, all based on work that was in things that were applicable to human health. So there was sort of a natural, if not technical, ability; there was certainly a natural comfort in biological systems involved in human health, as opposed to the other potential things you could do. In fact, when we played with the industrial side for a while with Genencor, we had to import most of those folk because we didn't have that many people that were even familiar with most industrial issues.

The third reason was clearly return on investment. With a colleague of mine, Gary Steele, we both shared the presentation of our strategy meeting that I mentioned at Silverado. I talked about the details of the projects. He, with a background at McKenzie and company, focused on the overall strategy. He had gone through and established that each of these programs was roughly equally risky in all areas and equally costly, up to the point of the molecular biology, which in 1983 was still mostly what we were doing. He reduced it to a simple mantra, that got repeated a lot after that, and I think he was right: it all takes the same amount of work, it all takes the same amount of luck, and it all takes the same amount of money. The only difference is, if you produce chemicals, you've got to sell them for dollars a pound. If you produce industrial chemicals, like enzymes, you can sell them for hundreds of dollars a pound. If you produce animal health products, you've got to sell them for dollars a kilogram. And if you produce human health products, you can sell them for hundreds of dollars a milligram.

Hughes: [laughs] Yes.

Gower: Another thing we did was to sell off the foot-and-mouth disease vaccine program to Bayer. But it was sort of a touchstone on looking back at things when we decided that pharmaceuticals is really what we're doing anyway. Let's just formalize this and get on with life. And yes, these are the five programs we're going to focus on. There was one left that was animal health, the rest were all human health.What would you do? This is all the same work, it takes the same degree of intellectual drive. If we're saying we're going to be the best at both the science and the business of biotechnology, what should you do?

Everybody kind of looked at each other and said, "What's to think about?" I don't want to make it sound too dramatic, like that was a real eye-opening experience. It was just the point at which we sort of stopped paying lip service to the fact that we were going to do all these things and said, "Let's cut the crap, let's just get on with this." That's the point at which we decided to put our industrial effort into a joint venture with Corning and form Genencor, and stop trying to make it exist within something that was clearly focused on pharmaceuticals.

[End Tape 2, Side B] ##
[Begin Tape 3, Side A]

Gower: Ironically, even our scientific success with industrial enzymes got in our way. In the late eighties, early nineties, along comes the merger with Roche. We get to the Federal Trade Commission folk, who were basically trying to see if they had any objections to Roche and Genentech merging, and lo and behold, one of the things they bring up is that Genentech owns this process that can make vitamin C production incredibly more efficient. And Roche dominates the world market in the industrial supply of ascorbic acid—not certainly in selling the final product, but in terms of making the bulk material, they own most of the market. So therefore, we would obviously have a circumstance of unbelievable market monopoly—somehow I couldn't think of us as the Microsoft of the vitamin C market, but we had to get rid of it.

The problem was, we couldn't sell it to anybody. [laughs] It's true: we'd already tried. In fact, in my usual unpolitic style, I offered to give it to the Federal Trade Commission if they would just approve the merger: "Here, you guys figure out what to do with it! We don't know what to do with it. It's been there for years. Yeah, okay, it takes a several-step fermentation process down to two, but look, here's the history." And John McLaughlin and the other lawyers at the time took them through the documents of our contacts with vitamin C manufacturers and said, "We can't sell it to anybody. They don't care."

So at the end of the day, in order to get the Roche-Genentech merger approved, we were required to sell the last remaining industrial enzyme process, which—oh, by the way, Genencor didn't want either originally—that we had done in those early days when all things seemed possible, except we didn't quite know how. At this point I was gone [from Genentech]; I was simply brought back to testify to the FTC, as I had said. But eventually, they got Genencor to take it. But to me as a knowledgeable outsider, it looked to me like one of those deals where they actually paid Genencor to take it; it just wasn't quite stated that way. And indeed, Genencor's never done anything with it since. The merger got approved; it went ahead, and that's the end of that story.

Looking back, I can't see that I would redo a single thing. I mean, you don't get everything right, but I think that's one that's pretty easy. I think that it was the right call to focus on human health. I think you'd find it hard to find many people that think it wasn't. It allowed a focus, it allowed a building up in science of some critical resources in immunology, in hematology, and in other areas that we probably wouldn't have been able to get away with if we had been spread across other areas. I'm really glad we did it.

Hughes: Well, good. I think we should stop for today.

[End Tape 3, Side A] ##
[End of session]

Interview 2, August 25th, 2004]
[Begin Tape 4, Side A] ##

Gower: We at Genentech ended up formulating what was done in the early '80s from a business development standpoint, and what ended up being utilized by some of the others [early biotech companies]. And it worked quite well. We're all doing different strategies now. But for the early part of biotech, it worked exceedingly well. Tom Kiley always liked this way to say it. He said that I came up with the phraseology—maybe I did; maybe I didn't. I don't remember. The mantra was, "Sell the product three times." We knew that from the early response of the U.S.-based multinationals that there was a fair amount of pushing-the-ball-uphill skepticism in the early days of biotech, as odd as that seems now.

Hughes: Meaning, could it really produce?

Gower: Yes. Could it produce? Not could it produce products, but could it produce products that were important enough to them? Would they be big enough? Would they be real commercial products? You've got to remember that the history of biological products, with the possible and in fact notable exception of insulin, was that they were kind of small products, not the sort of thing—with the exception of Lilly—that most people had much background in the pharma business. Now that's tremendously changed. But that was kind of how we were starting in the early eighties. We also knew that starting with human growth hormone, we felt that we'd be better off selling products ourselves. And it was really around that, and then later used for other products, that we evolved the strategy in my group of: there are plenty of midsize European firms that could do a fabulous job if we could talk them out of the U.S. market. They all say they need it, but there are a group of folk over there that if push comes to shove, and it looks like a doable product, they will license it just for North America. Likewise in Japan, at that era—this is not true today—most of the big companies would always say they had to have Japan. But with the exception of Pfizer, which had bought Taito in the '50s—and Merck hadn't even bought Banyu [Pharmaceutical] yet, just to put it in perspective—they all did it through distributors. So at the end of the day, they didn't like it, but if you took it away—it was taking away a third of the world's market—you could still get away with it. And then there was at that point in the U.S. tax code an ability to use limited R&D investment partnerships, so that people got a tax advantage deal. We could do basically the funding for the U.S. NDA [New Drug Application] by in essence doing the same thing that we, Genzyme, Amgen, so on and so forth did a number of times in the eighties, which was fund the U.S. development, which if you didn't look at it from a worldwide basis, you could raise enough

money in a limited R&D partnership to fund that. By combining licensing in Japan, licensing in Europe, which we weren't going to be able to deal with anyway in the early going, you could put together a consortium. [Gower added in editing: Building a Development and Marketing organization in the U.S. was expensive and difficult. Europe and Japan had to come later.] And we actually co-developed with those folk, at the same time we paid for the U.S. development. This was true of not only HGH, t-PA, gamma interferon, all the stuff that Genentech did in the early eighties.

Hughes: George Rathmann was a pretty experienced guy.

Gower: Yes. We did it first because we were there first. Growth hormone was approved, when was it? Four years before Amgen's first product was approved, and it worked. So I wouldn't hesitate to take anything that worked, and do it. There's no particular reason to think that if the situation had been reversed, Amgen wouldn't have ended up with the same strategy or one close to it. I don't think of it as copying; I think that we all kind of evolved to something that fit those times, but was very different than things that had been done in the past, from small start-up companies automatically licensing to large pharma and turning the whole process over to them. Instead, we would develop part of the programs, use a financing vehicle that was then available—is not now because of changes in the tax code and all sorts of other reasons—to finance the part that we could actually deal with anyway, and also—something you can't do today, because there are very few of those left—have large enough partners in Europe that we could rely on to co-develop with them, and in Japan, and have them stay still for only being licensed in their home countries. Some of the Japanese can still do that; the European's can't. The one's that are left, can't. There were a lot more then, though.

Hughes: My impression is that Genentech had a lot of activity in Japan.

Gower: Well, we did.

Hughes: Why was that?

Gower: Because it's a third of the world market for pharmaceuticals, and from the beginning part of the business strategy was, and it's sort of how this evolved: if you're not simply going to license what you invent to large global pharma—which we did in the early days, with insulin and alpha interferon, but—

Hughes: But you lost a lot when you did that.

Gower: Of course. We lost a lot of the potential returns of the product, but you've got to crawl before you can walk and before you can run.

Hughes: You were a baby company.

Gower: Exactly. So you do what you have to do. Bob, myself, most of us, wanted to hang on to more of these products rather than less. We were starting with things that clearly we could build a niche development and marketing effort around; this was not chronic disease sort of things that are a little bit harder to do. Those situations dictated this fairly natural progression, which was comfortable for me because I'd been used to doing it in prior life. Well, okay, then we've got to go find somebody to take care of the European and Japanese side of it, because if were lucky, we'd be able to do the U.S., but that's the end of that road because we just won't be able to develop ourselves as a global pharmaceutical company overnight. That's just not real. And from the beginning, it's just sort of traditional pharmaceutical logic that nobody invented, it evolved over the years, that you basically have commercially, three market areas for pharmaceuticals: it's Western Europe, it's North America, and then it's Japan. I wouldn't say you forget the rest of the world, but whatever happens in the rest of the world commercially doesn't matter.

Hughes: Well, that's changing as we speak, of course.

Gower: Well, I was talking about the 1980's.

Hughes: Yes, I know you are. But that's quite a revolution. I'm thinking of big pharma being pulled into the developing world.

Gower: Well, of course. And there is a lot still to play out, and a lot more changes to come. This probably gets too far afield from what you want to talk about, but don't mistake the whole issue of price and differential country pricing for commercial importance in terms of where one can make money. I once had a conversation in a fairly private setting with [Senator] Dianne Feinstein. She named something that costs less in Mexico, and I said, "Well, Dianne, Kenmore refrigerators cost less in Mexico. What are you talking about? If they don't cost less, you're not going to sell any. I mean, what is it you don't understand about this picture?" This is not a piecework sort of product trade where you're dealing with the cost of crafting shoes, you know? That's Nike's business. All the costs in this business is not manufacturing; it's R&D. And once you've recovered the cost of R&D, it doesn't matter what your variable pricing is, you're going to cover it. Anything above the cost of manufacture adds. So the issue is, who pays for what? And we're now in the midst of that full time. Luckily biotech is not in the crosshairs

The U.S. taxpayer and to a lesser extent the European taxpayers have been for decades now paying the cost of the development of pharmaceuticals. I'm sorry; I left out the Japanese. And when they go about evening the pricing systems in France and Germany and the UK and Japan where you have the government set the price, but they have a research based pharmaceutical industry in those countries, it isn't as different from the price in the U.S. as the Canadian price is, much less the price in the third world where they can't even afford to get the

doctors out there, much less pay the cost of medication. So it's a very, very complex problem. Everybody needs to do a better job of making sure that there's access to medication, which in my simplistic way of thinking is the real issue with some of these drugs. I think that goes without saying. Most of the biotechs I know—and it's certainly true of Genentech back when, and I think Merck was the first big pharma to do this—if nothing else, give it away. Merck was the pioneer with this; not any of us folk: they had a drug called Ivermectin—huge, huge animal drug that was an antihelmintic, an anti-parasitic. Parasitic diseases are not a big deal in the developed world, and so it was never developed for human therapeutics in a big time way in the U.S. But for things like river blindness and schistosomiasis and other third world-only types of things, this can be a major, major, major innovation. So they actually went to the costs of doing the studies—they knew they weren't going to get paid for this—and got it approved. Merck worked with the WHO [World Health Organization] on it; [quietly] phew, those guys are interesting. And when it came right down to it, it was fairly clear that nobody in equatorial Africa or equatorial South America, which is where those diseases are prevalent, could afford it, so they just gave it away. Even then, most of it went out of date sitting on the docks. But it's the same thing with HIV.

This whole conversation is so silly, because people want to believe whatever they want to believe, and in this increasingly politically polarized world—well, certainly here—they start with a premise and then set out to pick the points that will prove whatever they want to prove. Thank God I'm not in the HIV drug [business] so I can be at least somewhat unbiased, but selling into the developing world is hopeless for the big pharma guys. Because even if they make them available for free, they're not going to be used. You just know it. TB's a bigger problem, for god sakes. And they're not even getting the already generic drugs that people need for TB. Malaria's a *huge* problem. More people die of malaria die in Africa then of AIDS. What about that?

[End Tape 4, Side A] ##
[Begin Tape 4, Side B]

Gower: Africa's got so many problems, it's not funny. You've got scattered cases like Uganda; they've done a great job with HIV. But it started with putting nurse practitioners and doctors and access to medicine in place first. Doesn't do a damn lot of good to have the drugs there—

Hughes: If you don't have the infrastructure.

Gower: Exactly right. So it's a little hard to talk people into lowering the price on HIV medications when you know what's going to happen is its not going to be used there; it's simply going to be trans-shipped and sold somewhere that it would have sold for more otherwise. That's the cold commercial fact. And that's what all these fights are about, which is never the way it's taught. So we're getting to

an area where there's going to be more uniform global pricing, and then we can do another way to transfer payments from the developed world to cover the cost of R&D in drugs, should we want more drugs for R&D, which is they'll be at a more similar price, and we'll simply give them more in government subsidies to pay for them. It's a fascinating business.

Hughes: Back to Genentech, nonetheless. We talked last the time about the curtailment of the vaccine program. I asked a two-pronged question, but we never got to the second prong, which was antibodies. In the early 1980s Genentech was working on antibodies and, as I understand from talking with Herb Heyneker, there was promise there, but Genentech did not emphasize the program until later. Of course antibodies have become the basis of many of Genentech's most recent drugs. Do you remember anything about that program?

Gower: Of course. [pause] Certainly Herb's comment is accurate factually, but it ignores a whole bunch of practical stuff like, antibodies had promise just like cloning had promise, but clone what? That's an important question. There's a patent Genentech holds, which is the Goeddel-Heyneker patent, which was on the first chimeric antibody, which then led to humanized, et cetera. So that's why Herb feels close to it. We tried to figure out—yes, but what? And at the time, there were serum immune globulins and the like, but that's a pretty weird business. Even in this day of a lot of antibody companies, not many people are taking that one on. And so it took a while. In fact, Genentech and a former Genentecher, Bill Rastetter at Idec, were responsible for pulling the promise of antibodies in the mid-eighties, which was hot, out of the disappointment of antibodies in the late-eighties, early nineties, and making them hot again, with Rituxan. Until Rituxan, there was no genetically engineered antibody product that anybody would write home about. Zippo.

Hughes: When did that come in?

Gower: Mid-nineties. Now that's turned out to be a major drug. Either that or Taxotere, depending on the year, depending on the use of the data, is the biggest-selling cancer drug. But until Rituxan, the investing community had pretty much turned off on the idea of these antibodies that were much hyped in the mid-eighties as magic bullets for cancer and all sorts of things as being worth much. And that's because people had gone after naked antibodies against tumors only to find that the markers on tumors were very heterogeneous, and all sorts of other stuff. So like everything else in this world, its one thing to know how to do it; it's another thing to know what to use it for, and it took a while for the industry to figure out exactly what to use these things for. I remember conversations in the late eighties—well, Herb would have been at Genencor then—

Hughes: Yes, he was long gone.

Gower: —with Art [Levinson] and Dave Martin, and lots of us. And Art and Dave Martin pretty much leading the charge in terms of, well what would be a good target? And that's when the ideas like anti-IGE [anti immunoglobulin E], actually HER-2 was their approach, it just so happened it worked like a charm. It's a smaller market but that was actually the first personalized medicine, if you want to look at it that way. That's a marvelous, marvelous research story, and we're going to see a lot more of this. But in terms of commercial importance, Rituxan was the first commercially important antibody. It was developed by a group of folks that had it spun out of Genentech and formed Idec, and Rituxan was commercialized by Genentech. But that didn't happen until '95,'96,'97, somewhere in there. So Herb was right; he was just off by fifteen years in terms of when you could have done anything with the technology.

Hughes: Was this often a problem with the scientists? That they had a way to do something, but you development and marketing people had to come in and say, "Yes, but what is the product?" And on what time scale, and with what resources, and where's the market?

Gower: I think one of the real strengths that we had at Genentech was that, although all of us were very strong individuals and very opinionated and all that, we all went pretty well together in terms of sorting through this stuff. A lot of arguments, but a lot of friendly arguments. You mentioned with the vaccines: Dennis Kleid, a wonderful guy, but beyond those early days was never part of any strategic discussion that I can remember, and Herb, who's a wonderful guy and a good scientist, but was not part of those discussions because he didn't think that way. But you had the Dave Goeddels and the Art Levinsons and the Dave Martins and the Larry Laskys who were *pure* scientists but were just as interested as I was or the medical guys were in working on something that fit.

Hughes: The product.

Gower: Well, no. That fit all of the pieces together—the technology, the medicine, the markets. I actually think that one of the strongest things Genentech had going for it—and Bob [Swanson] really insisted on this, not that he really had to, most of it was in the people he hired—that all of us were very interested in—I mean, I could walk into the labs and understand what they were talking about. I understood medicine; the medical guys understood the science and the marketing. As I think I said to you last time, Levinson particularly, but even Goeddel, asked tons of questions and really wanted to understand what the hell we were talking about when I said, "This was this kind of market; that was that type of market." We ended up making those guesses together, which sometimes they are when you're dealing with completely novel products. And it didn't always include every scientist that was involved in the programs. I think two of the key examples [who were not always included] would have been Heyneker and certainly Dennis. Dennis thought we ought to do vaccines; it's just that none of the rest of us did. But it wasn't like it was a commercial decision versus a

research decision. Ask Art. Vaccine development just didn't make sense compared to the other things that we could do. Where we were trying to look for the most part is, where are the things that cover more of the bases rather than less, in terms of the technology to discovery? Much more important I would say than just the ability to do it in this business, and the ability to market it is a medical need. If you don't start there in this business, you've made a real mistake. You really have to understand that.

Hughes: It came naturally to you, I would think, with your background, but it wouldn't come naturally to a Heyneker or a Kleid who had come fairly recently from academia.

Gower: Sure. But there were plenty of people at Genentech who had also come fairly recently from academia that it did come naturally to.

Hughes: Why was that?

Gower: I don't know. Different personalities, different perspectives.

Hughes: Are you thinking of Levinson?

Gower: I think of lots of people. I think of Levinson. I think of Dave Goeddel. I think to some degree of Axel Ullrich, who's every bit the scientist they are. Some would argue they've got a lot more publications. But that's not actually my point. It's just that some people thought and were more interested in the broader scope of not just the technology but how do we turn this into a useful product that will mean something for healthcare. And some did, some didn't. And I think that's across the board, from science to medicine to marketing. But in general, I think we had more people that were comfortable in straddling the line, one foot in each world, than most organizations had at that time. I think it was one of the real strengths of Genentech, and I give all the credit to Swanson because he basically insisted on everybody talking about this stuff. He couldn't fathom the idea of somebody saying, "Well, those guys won't do this or those guys won't that." That's big company stuff, and we're a small company. Let's get down and decide together and figure out how to do this stuff.

I think I told you the anecdote last time: I was actually floored in one of my very first meetings in my first year at Genentech—it was Levinson, but there were others too, who wanted to know the potential market for something before they wasted too much time figuring out how to do it scientifically. So yes, there were a few people like Dennis and Herb who just didn't think that way, but there were many more people who were equally good scientists—starting with Dave Martin, who was VP of research, and Art and Dave, and Dick Lawn and Axel Ullrich and lots of people, who actually were not only more willing, but actually quite interested in having a say in terms of the downstream stuff as well. And it was really fun. Really fun. I'd never experienced that in big pharma, to have that

much involvement across the board. I think it made all of us more on top of our game—for my people to have to defend marketing strategies to the scientists. And for the salesmen, at least those of us on the business side, to be able to talk to the guys in the lab one-on-one. Not just the guys that were in charge, but the guys doing the work, and understand it, and know what was going on. Likewise on the clinical side: should we really be doing the studies towards this, or is the ultimate goal really to get something like that? And it was all very, very, very much that ability of a small company with people hired of more or less a like mind—self-selection—who thought like Bob Swanson, that you ended up—Sometimes for all the science you put into it, you're really guessing, and at least we guessed together. Sometimes it was wrong, sometimes it was right. But the vaccine decision, no matter what Dennis thought then or thinks now, was not an issue in which the commercial guys thought one thing and the research guys thought another thing, depends on which research guys you ask. Art didn't want to do vaccines. [laughs] Otherwise he would have never come with me on the trip to Merck to sell that hepatitis B vaccine, which I think I also told you about.

Hughes: Yes. At Genentech's start, the criterion for hiring was: can we find any good scientist who can do this new technology? You could say that Swanson and Boyer were lucky to get a Goeddel, who could do the science, had the golden hands, and yet was wedded to the idea of getting quickly to a product. But as the technology became more available and the people doing it, were you looking to hire people that had the technology that Genentech needed but that also had the right philosophy to go along with it?

Gower: I think that most of the folk that [Swanson] had something—

[End Tape 4, Side B] ##
[Begin Tape 5, Side A]

Gower: —whether they thought that way or not. Because otherwise they wouldn't come work for this crazy guy, if you follow me. There is a self-selection process going on here. The foremost proponent of this—he was the most vocal—I always thought was Dave Goeddel. I remember very early on, him being very forceful with folk in molecular biology—we had lots of scientists, but most people in the early eighties at Genentech were in molecular biology—and saying, "Yes, that's really interesting research"—and do I remember names, but I'm not going to name them—"that's academic research. If you want to do that, go to the university. We can do great research, get it published in great places, and also make products that matter. That's what you ought to focus on doing." So yes, that attitude wasn't just Swanson's, but certainly it started there. But then after not too long a period of time, you ended up with a corporate culture where that's what more people than not thought. Everybody's important, but the ones that could actually make the decisions were even more that way—like the Goeddels. And it really was such an important part of the Genentech thought, philosophy, et cetera, that yet more self-selection occurred with younger scientists that were

hired. It wasn't like we sat down and gave the HR [human resources] guys—I don't even remember the HR guys being involved—it was more just that was the type of people who would be drawn to this type of corporate approach, and they reinforced it with the people they hired. And yes, I remember Dave especially—I don't exactly remember Art doing this, but it wouldn't surprise me because I know he thinks this way—being absolutely a bear on stuff like this: this basic science you're interested in is really interesting stuff, but if that's all you want to do, then why don't you just do it at the university? If you can't think of something that will end up being a pharmaceutical product, that would do people some good as a medicine, then why do it here?

Hughes: What happened to those people who couldn't adapt?

Gower: Some of them moved to the university. Did quite well. Peter Seeburg came as a post-doc from [Howard] Goodman's lab [at UCSF] and went back as a Herr Professor Doktor at Heidelburg. Now, Herb [Heyneker's] kind of a special case because he liked a lot of things. One of the things he ended up liking was what became Genencor, so he went there. Still commercial, but that happened to be commercial that happened to fit his ideas, so there you go. Wasn't drug, but that's ok.

Hughes: I was surprised when you named Axel Ullrich amongst the people who had a marketing mind, because I had gotten the image of him as being much more a scientist than somebody market oriented.

Gower: He wanted to have it both ways, and he's good enough that he found a way to do it. He's had a part in starting up about ten companies. Axel is a special case that doesn't neatly fit into any category. I remember Dave saying words to the effect, "Yes, but unlike—again without naming names—most of these guys who say they want to do academic research, Axel can actually do it!" He's good enough to have around just for the covers of *Nature* and *Science*. Axel was totally in sync with the idea of Genentech focusing on commercial products, and sometimes it fell into things that were his research interest and sometimes it didn't. But Axel is one of those wonderful people who can thoroughly believe in the concept; he just doesn't necessarily think that it pertains to him. [laughter] But it was a strength. I really mean that. Did we have a direct use at the time he cloned them for epidermal growth factors—no. Now if we could fast forward twenty years to today, and you've got Tarceva, which is their drug, and Iressa which is AstraZenica's, maybe we'd be somewhere. But nobody at the time quite knew how that worked. Axel became the first to clone a human receptor, with insulin and then with epidermal growth factor. Axel and Dick Lawn later figured out how part of that system worked with atherosclerosis. In the meantime, there were *Science* and other major articles left, right and center.

But the flip side of that is, Axel also had a lot to do with these discussions I was talking about, and sitting down and working out which programs would get what

priority to do what. He had no problems understanding the need to target something that would be drugs. He was pretty good at separating what the company ought to be doing as opposed to where his individual lab fit in. If it fit into something which was purely commercial, he didn't have a problem with that. So Axel's a very interesting individual, and there was never an issue that I remember with Axel in terms of him not getting it commercially. Sometimes that didn't fit with what his lab was doing, but it worked out just fine because he was willing to both take part in all those decisions that allocated all those resources. He clearly decided that Dave and Art Levinson were the important scientists in terms of decision making. His commercial bent is pretty well-established by what's happened since then. And he's really, really good. We just used to kid that Axel was probably personally going to lose interest in doing the research after the first publication, so it'd be a real good thing to have another lab working on it too. [laughter]

Hughes: And that usually proved to be the case?

Gower: Yes.

Hughes: He was on to the next thing.

Gower: Yes. That's a very different thing than, I'm going to do animal vaccines, or die trying, [laughs] and drag the whole company along with it. I'm not trying to dump on Dennis; I like Dennis a lot. I don't think Axel fits into that category of folk at all. Otherwise he would have never started up Sugen; he would have never started up a ton of the companies, most of which are in Germany. In fact, he wouldn't have insisted that the Max Planck [Institute] let him do that, which was a big deal at the time that that was done. That's not very German, in terms of the mindset of German academia. But he told them he wasn't going to come back unless they allowed him to take some of the discoveries that were "owned" by the German government and license them to people that'll do something with them, and that it was okay if he took part in that. Pretty heretical at the time for German academia.

Hughes: When you look back at pharmaceutical industry history, you see interaction between German academia and the pharmaceutical industry, but I guess there was a clear separation. Professors didn't have their feet in both camps, which I think is where the controversy both in Germany and here originated. If you were a professor, you shouldn't keep your position in academia and simultaneously become a CEO. It was combining the two that was seen as the problem.

Gower: People got tired of debating it because it was obvious where the world was going. Well, Paul Berg spoke out against Boyer being part of the founding of Genentech, and later he founded his own company [DNAX]. So at a certain point you just stop this nonsense and get on with life. The engineering professors at Stanford had been doing it for years; how do you think Silicon Valley was

built? But it was a novel concept when biotech first got going, but we dealt with it here in the States first. By the time Axel went back to Germany, they hadn't dealt with it, and he was just bringing what he had seen and sorted through on his own in the States.

Hughes: Let's talk about Kirk Raab, who arrived at Genentech in 1985 as chief operating officer. Do you know anything about his selection? There are plenty of pharmaceutical executives out there.

Gower: Oh, we went through a few. That was a long process. I think—now this is just my guess—that Bob [Swanson] had to struggle so much in the early eighties with the folk at large pharma that didn't necessarily believe that biotechnology had really much of anything important commercially to do with the pharmaceutical industry. I remember very well, in fact I have kidded with the Pfizer people about it since, Swanson and I having breakfast in New York with Jerry Laubach, who was then CEO of Pfizer, and him saying that he didn't believe in biotechnology. I remember Bob took it seriously. But that was fairly common in the early eighties. So going up to '85, Bob viewed it, I think—and I was there with him for a lot of it—as a constant struggle to show that it was more than a technology, but an important way to come up with new drugs etc. And I think he felt that it would be better for Genentech if we had a person who clearly had run at least a big chunk of a world pharmaceutical company who would be voting with his feet, if you will, and it would help us with Wall Street, and it would help us with pharma, etc. And that was kind of his mindset. I don't remember exactly how long we ended up interviewing folks, but it wasn't a short period of time. We had a lot of people come in from the various headhunters that Bob had hired to do this stuff, and Bob also made most of us, many of whom you've talked to, part of the interview process. So myself, and Bill Young, and Dave Goeddel— Art I don't remember, but probably Art took a good chunk of it—Dave Martin were all part of the interview for these guys too. I think it was a matter of two things: first of all, it was fairly hard in the initial vetting process to find someone who had run all global pharmaceutical operations in a large pharma, and been in those kind of roles. and was comfortable with that kind of an organization. I mean, just human nature. So a lot of the more traditional big pharma folk just didn't fit. They'd been in some silo of some functional note or another; I mean, they were head of medical, or they were head of marketing, or they were on the legal side, with forty years of their career before they finally got to something that approached a COO. And most of those guys really were not well received by most of us and vice versa, because they needed a lot of people with a lot of specific knowledge to make them effective. And Genentech wasn't that kind of place; it needed a more hands-on person. And I think its not surprising both for ourselves and for others in the industry that it tended to be the folk out of the more diversified companies like the Abbott's and the J&J's [Johnson and Johnson] and the like where you had a lot of people that were of a different background, mindset, that had to cross over lines in getting to where they got to. So Kirk, as did at least one

another I shouldn't name, fit quite nicely with that mindset. Kirk had been in general management; he had been George Rathmann's boss. He understood marketing of heavy-duty prescription pharmaceuticals from when he was at Pfizer; he had done the international part of that. So it was a broad, hands-on type of experience he brought to it. I think that that made a lot of us comfortable that, well okay, if you're going to do this, you might as well get somebody that doesn't need a cast of thousands to tell him what this means. We'd all had the experience, either on our own in big pharma, or in the cases of some of us going back—Goeddel and I to Roche when we were doing the interferon programs with them in the early eighties—of J.J. Burns who was president of Roche research, listening to some of the presentations and turning to his administrative aide and then saying [whispering], "Is that good? Is that good?" [laughter] Dave and I would just look at each other and roll our eyes. I mean I was a commercial guy and I knew, and Dave was a scientist and he knew, why didn't this guy know? So that was the first piece of it, and I think the second piece, which turned out to be a miscall, was: could he and Bob coexist? Now that wasn't our decision; that was Bob's decision. I think Kirk was fine on the first piece. It was the second piece that was the problem.

Hughes: And you hadn't predicted that?

Gower: I hadn't even tried. I figured Bob and he could figure it out themselves whether they could live together. I'd only tried to figure out whether I thought I could live with Kirk, which was the question Bob asked me. And I could and I did. He didn't ask me how I thought he and Kirk would get along. I don't think Kirk was a bad choice given what the reasoning was and all the logic we went through. I just think it's very, very tough, especially in a start-up organization where founders tend to think of the company and themselves in almost interchangeable terms, that you run into some issues and some conflicts, and that's that. There were also some personal characteristics of Kirk that didn't show up in a big way until I was gone, so I don't really have much to say about that. But Art probably does, and a few others that had to deal with it. I mean I didn't have a problem believing it. Until Bob was completely out of the way, none of that stuff ever was problematic because Bob kept it in check.

Hughes: You're thinking of some of the things that eventually hit the newspapers?

Gower: [Signals agreement.]

Hughes: Well, it's a tough call isn't it? Having to deal with a founder and a strong one. Swanson was creating a company, but in a sense he was also creating also a model for what was to come. It's a difficult act to follow, and to follow it happily.

Gower: If we look at other early biotech CEOs, I think you'll see that most of them failed [laughs]. So it's a tough one. And this is not just true of biotech. I've

heard from VCs [venture capitalists] that it's a constant issue in start-up companies. Although everybody is genuine and means well in terms of how the division of responsibilities will be shared and so on and so forth, it's just very hard to make that work in an environment where, as you said, somebody is so closely and personally—from their side and the outside—identified with the company, the industry. It's really tough to make it work.

Hughes: I understand that one of the reasons Raab was taken on was to build a national marketing operation.

Gower: No, really that was pretty much done by the time he arrived.

Hughes: Was it?

Gower: Well, ask [Thomas D.] Kiley or somebody. But Gary Lyons [in marketing] and I had pretty much started that process.

Hughes: And it was pretty far along?

Gower: Oh, it was pretty well done.

Hughes: Was it far enough along to handle tPA for the huge market you projected?

Gower: Sure.

Hughes: It turned out to be not so huge a market.

Gower: Does Kirk deserve some credit for Genentech building the commercialization of it? Sure.

Hughes: But he didn't start from scratch?

Gower: I would say the two people he left alone the most were myself and Bill Young. We both had great relationships with Kirk because he basically let us do what we did.

Hughes: Recognizing that you knew what you were doing.

Gower: Exactly. It's not that Kirk couldn't have; Kirk was very comfortable with both areas but decided that his personal focus was on things like building the project teams and making sure that we had a strategy that had us not just pursue lots of different directions at the same time. Goeddel always said when we worked together at Tularik, and later we talked about it on a couple of occasions, he was happy on the research side if we could just stop talking about the budget forever, and somebody could just set a number: here's what you've got to work with, go! *Now* tell me how you're going to spend it. Whereas Bob's approach was

probably, for the point we were in the [company's] evolution, a little to all-inclusive. You can't just openly talk about this stuff forever; you've got to decide some stuff and go on. Kirk clearly had more experience at managing that sort of stuff. But I believe it would be accurate to say the two groups he left alone the most were manufacturing and the marketing group, because it was mostly done. Kirk and I didn't think all that differently about how to do this; that's one of the reasons we got along well. That was a non-issue. From the standpoint of the broader issue of convincing pharma that we were serious about marketing our own products, or Wall Street that we could market our own products, that it's certainly more believable when you've got somebody that has done that who's in charge of the company. But the strategy, the sales force, was pretty well built by that point. The major last impediment to building the rest of the sales and marketing effort was a lot of companies wanted a piece of tPA and wanted to market it for us. This was all pre-Kirk. And Bob at least wanted to listen to them. Probably for my own personal reasons, but I thought I was being objective too, I didn't think it made any sense; they weren't going to do anything that we couldn't do. But once that was decided, and indeed until Kirk was sure that we were serious about that [Genentech would itself market tPA], he probably wouldn't have come. [laughs] I think he would say that. Why would we want to come? So no, we were already in the process of doing exactly what we did for tPA, and, as I said, from a functional standpoint on my stuff, Kirk and I got along fine.

Hughes: So what was he doing, if he wasn't building a marketing organization from scratch?

Gower: Some pretty important stuff. The things that Bob had not done. Chief operating officer in his case really described a lot of the stuff [he took charge of], just integrating all of the functions in some true, managed way. I referred to the budgets, but I wasn't just being flip. How does this all stuff fit together? We at that point were, I don't know, a thousand people? It was very different then when I got to Genentech and there were thirty-some odd people. You have to have a process; you've got to have an actual management in place that knits all this stuff together. That involved putting in systems that, for instance, ended up—and this was great—having the financial guys actually second fork over into R&D, manufacturing, marketing, because we were setting up systems—in my case, for customer order entry and the like—[in which] we just needed much closer coordination than two separate functions. So here's a way to do it I've seen work, in fact I used this in Mexico when we started up the international organization for Pfizer. You guys need to take one of your smartest MBA/CPAs and just give him to Jim, and just let him use that to set up the customer order entry system. We're never going to do this if we're not looking at it from a common viewpoint. So there were a lot of practical things that he did. I would say one of the most important was to get things started—as I said earlier, project teams probably don't quite do it—in terms of an integrated strategy. Of all these great ideas, which ones do we pursue and how do we manage that process?

Because that's cross-departmental. We were getting to the point where the handoffs from R&D to process scale-up to manufacturing to clinical were more difficult than they used to be; all that was getting more complicated.

Hughes: Because it was large, it was impossible for any one person to know what was going on in the company as a whole?

Gower: It needed to be more systematized, and you had to put in a more formal management process. Kirk had actually *done* this; he had *lived* this. Bob had never been part of anything like that.

Hughes: And probably it wasn't his major focus, because wasn't it you that told me, that as far as you know, there was never an organization chart?

Gower: Oh, I happen *to* know [that Genentech didn't have one.] I remember having to rush and put one together that actually fit, more or less, the current organization when we did the merger with Roche.

Hughes: It was an afterthought.

Gower: Well, it wasn't so much an afterthought; we knew this. Let me just say that although we had organization charts, we never actually bothered until almost the merger to try to make them fit the real world. And nobody ever paid any attention to them. And a large part with that was Bob.

Hughes: You said, the titles didn't really describe what people did.

Gower: [Gower agrees.] Bob was much more dependent on the informal organization than the formal. And the best example of that, or the worst, depending on your viewpoint, was probably Dave Goeddel. Dave was more important than most of the people who were organizationally more senior than he.

[End Tape 5, Side A] ##
[Begin Tape 5, Side B]

Gower: Some of the folks—Rob Hirschberg comes to mind—that worked for Young, trusted Bill implicitly. He thought Bill was great, and Bill was great. But he happened to know that it was going to be Raab that figured out exactly how we got this done in a way that nobody had ever done before. So you know Bob was really much less interested in the hierarchical, and much more interested in, well, who's doing the actual work, and blah, blah, blah. Same thing with my people. So Kirk, while being fine with that, also knew that at a certain [corporate] size, one person can't have their hands so thoroughly into all the inner workings. You can't make organization-wide decisions that way. And so Bob realized that. Bob wasn't dumb; he got it. But it's all of that more general stuff that I think Kirk did, and was the role that Bob wanted him to serve.

Hughes: Where does [Fred A.] Middleton fit into this picture? Am I right in thinking that Raab was a successor to Middleton?

Gower: No, not at all. Fred was there at the start and was a friend of Bob's out of college and was the first CFO [chief financial officer]. But Fred was not even there for all that long. Fred was long gone before Kirk ever got there. And he had been replaced at least twice that I can think of in terms of CFOs, first with Pat McGrath, and secondly with [Louis J.] Lavigne, who's still there. Pat with her significant other at the time moved back to Boston and started up companies on her own. In fact, she still does that. In the interim, people like Brian Cunningham and I ended up running Genentech Clinical Partners, which was financial. Fred would have probably done it had he been around. But Lou was still too fresh out of being an accountant that it didn't make sense, so I ended up doing that as president of the Genentech Clinical Partners. So Kirk wasn't hired to fill Fred Middleton's slot; Fred was a CFO, not COO, and Fred would *never* have been a COO in anybody's imagination, even Bob's.

Hughes: Why do you say that?

Gower: [pause] He didn't have any of those characteristics that I said Bob felt the need was for.

Hughes: The organizational skills?

Gower: He had never run anything in an organization; he had never been part of pharma; he had never— He didn't add any of that. He certainly had the financial skills to do the CFO part. Kirk's role was radically, radically different, and he had a whole different set of backgrounds.

Hughes: And so Raab was the first to ever have the title of COO?

Gower: Raab was the chief operating officer and was hired as president and chief operating officer. No one else except Bob was ever president, and no one else was ever chief operating officer, and Fred was just the first CFO.

Hughes: Okay. Thomas Perkins in his oral history says that *he* spent years, on and off, during the Raab-Swanson period trying to keep the two talking to each other.

Gower: Oh, he did, yes.

Hughes: How aware of that were people like you?

Gower: Very. Very. [laughter].

Hughes: Well, tell me about it.

Gower: I don't think you can find any of us that were part of top management that weren't. I mean, it varied depending on the circumstance. I really like Tom Perkins. Tom, because he wasn't just a venture capitalist but had actually built parts of businesses, did get this stuff. He understood the natural pressures on both sides, right? He had worked very closely with David Packard in building the computer business for Hewlett-Packard before he became a venture capitalist. He had had the experience—if not in the pharmaceutical business, which he has now—but in terms of management, some of the organizational issues, and so I think he understood the difficulty for both of them.

Hughes: Yes.

Gower: I mean, yes, he tried. I saw him do it in some smaller group settings, and I saw him do it in terms of either comments or complaints that I would hear from both Bob and Kirk in terms of, "Well, Tom says we ought to blah, blah, blah, blah, blah." Yes, I saw the visible role, and I think Tom had a very positive impact. At a certain point, after we'd been through maybe one too many—-well, not necessarily encounter groups—but outside professionals coming in for team building, which was really an exercise in Bob and Kirk building. Because the rest of us were along for the ride. There weren't any other problems to deal with. It just became obvious that the problem was a little bit more difficult to fix then that. But Tom really tried hard.

Hughes:

I would think that because he was more distance from the company than you were that it gave him an advantage, too.

Gower: Tremendously. And he had seen this particular thing before. And since he was both Bob's and Kirk's boss, he was in a much better position to fix it. I think he really tried hard, and in a different circumstance it might have worked. I don't see anything wrong with what Tom did. Yes, he did spend a lot of personal time trying to fix that.

Hughes: Do you think that the tension between the two principals ever interfered with Genentech's function?

Gower: Yes.

Hughes: Can you give an example?

Gower: [Long pause, sighs] Well, the area that in the late eighties all of us felt the need to pay more attention to was of the potential things that are going to follow up from the t-PA and the gamma interferons or whatever, how are we going to get a handle around the management of research? I don't mean the rest of us managing research. We had at that point tinkered with and changed the

management structure of science a number of times, most often than not dysfunctionally. And part of that was because, and I said, Kirk wasn't spending a lot of time focused on me or Bill Young, and he wasn't spending a hell of a lot of time making sure that the books were accounted for right. The most important strategic issue, really—there were a couple of others—was gearing up research for the next wave of things to come. And I think that Bob really felt that that was his turf. That tended to be where they locked horns the most. I can't say that it specifically slowed us up, but I feel that way. In hindsight, it's always easier. I didn't necessarily think this at the time: but how much better it would have been if we just went on and appointed Art sooner rather than later and just got on with life. Or, alternatively, [appointed] someone else. But let's stop screwing with it; let's just do something we can live with and give it enough time.

Hughes: Do you think that was somewhat the founder factor? Getting rid of a founder is a big deal.

Gower: [long pause, sighs] Well, one could make the case that that was not the right move, too. I'm not sure the exit of Swanson added anything. And I know some things which it certainly caused which in more honest moments Kirk would say might not have happened if Bob had still been there, that came to reflect back on him. Bob wasn't a problem; it was process. I really mean this: it was the two of them together that was the problem. In that context, if you can't fix it, then one's got to go. And I think that for lots of reasons, the one that went was Bob. And hindsight made it fairly obvious that, well, hmm, one could debate that decision.

Hughes: Well, looking at what came next, you certainly could.

Gower: Well, some of that you could see coming. Not all of it. But never in my wildest dreams, and I thought I knew Kirk pretty well. I was gone, long gone by then. But when I heard what happened [laughs] with the stuff after the merger with the Roche guys, and the second time around and all that, I said, "God, Kirk, what could have *possibly* been on your mind? I mean, just really, get a grip." I said that to him actually, but I was gone. [Gower left Genentech in 1992].

Hughes: Did he have any response when you said that?

Gower: Yes, he said he screwed up. He should have thought of a better way to get at this, or words to that effect; I don't remember his exact words. I didn't dislike him; I liked him. But I thought that he had some issues that got in the way there, and therefore got in the way of Genentech. But at any rate, back to your question, the getting rid of the founder part: [sighs] it came to that because neither of them together could find a way to work together, and I kind of always viewed it as both of their jobs to figure that out. Instead, at the end, at least the end when I was there, it got so a few of us ended up having to walk all of ten feet between Kirk and Bob's office and communicate because they couldn't talk to each other. I hated it. I used to tell them, "You don't pay me enough to be a

babysitter. I got better things to do with life." And that's why I said I was leaving—well, it was one of the reasons. I was also just tired after ten years; that was a long time at Genentech. I was willing to stay and do the merger, but I was originally going to leave about a year earlier. On the one hand it was good that I stayed because I got to do a lot of things that Bob or Kirk would have done. They kind of trusted me to go do the thing, they didn't trust the other guy to do, if that makes any sense.

Hughes: Yes. But that's not the way you want to go into something, is it?

Gower: No.

Hughes: By default.

Gower: I and others—Young, McLaughlin There were some of us that both of them trusted, and then there were the areas that they were pretty sure weren't quite right, that they could never agree amongst themselves about what to do about them. And that was a problem. So the whole thing can't really be taken much further apart in terms of parsing than simply, the chemistry issues got in the way, and got in the way for longer than they would have ideally in terms of allowing Genentech to move on to the next thing it did. That eventually happened; didn't kill anything.

Hughes: Levinson becoming president and CEO, you mean.

Gower: And it could have been someone other than Art. Although I think that Art—now this is clearly retrospective—was a *fabulous* choice. I didn't debate it at the time, although I was gone when that happened. But it made sense to me. If they had just decided on a decision and stuck with it, as opposed to second guessing each other. This was not important per se, but it was emblematic: Bob hiring David Botstein, world's most famous genomics professor from MIT, to be vice president without portfolio in research. Huh? [laughter]. It was Bob's way of still having a role in that, while Kirk was trying to sort through how is that actually managed. What a friggin' nightmare. It was just one sort of queegy thing after another. David Botstein was a very bright guy, but he never added a god damn thing in that context. In fact, that act, not him personally, just sort of making it even more diffuse in terms of these decisions, was really bad. It undercut Dave Martin at the time, and it undercut Art. I mean, let's get on with this.

I remember clearly one of the research clinicians saying, when Botstein had made one of his typically overarching comments about something to do with clinical trials, about which he knew nothing—We were in some meeting, and Bob repeated his favorite line: "But you don't understand; he was the smartest guy at MIT." And Elliot Grossbard said, "Well, could we return him for the second smartest guy and three draft choices?" [laughter] And Bob, god bless

him, laughed. I mean he was always able to laugh at himself, and that was a wonderful characteristic, god bless him. And the rest of us were just falling on the floor laughing. The problem wasn't Botstein; the problem was those guys not working against each other but deciding jointly and just sticking with it and getting on with whatever it was to be. But I mean it was nuts. Just nuts! How can you have one guy hiring someone to report to him to run research when you told the other guy to fix the problem and run research and nobody knows why this guy is being hired. I don't care who he is. If you just wanted scientific eminence, how about Boyer? Anybody!

Hughes: Well, let's get to the actual Roche story. Was one of the impetuses the fear of a hostile takeover?

Gower: It certainly was mentioned from time to time.

Hughes: If that were the case, why was Genentech in that position; I mean, what were the circumstances within the company?

Gower: Well, I think that there was the concern—I think we talked about it last time—with a couple of the prominent product candidates we had looking not what we wanted them to be in the clinic. Growth hormone was better than expected; t-PA was about half as good as expected. You can't drop two products out of a hopefully four-product company, but actually still a two-product company.

Hughes: Had gamma interferon done anything at that point?

Gower: No, and never did. We got an [FDA] approval, but commercially that was meaningless. That cost us money.

Hughes: But you had expected it, of course, to be profitable.

Gower: Exactly. And t-PA. So it is not unusual when you look at pharma that the pipeline when it comes is always a problem because these things are risky. Each drug you put in the pipe, something's going to surprise you, sometimes good, sometimes bad, but it's a risky business in that respect. The concern was not immediately having the next thing visible beyond t-PA. Two things had failed and at that point; we really had no idea what the next thing would be, which was why I made the comments early about it would have been nice if we had just gotten on with it, with Art—somebody that knows what they are doing and move on. But the concern was that Wall Street always being, well, what have you done for me lately? would reflect itself in us dropping in market value and being a very attractive takeover target, and so on and so forth. So that was the genesis of that comment. My own personal opinion, but this is purely personal, was that that really didn't have a lot to do with [the Roche deal]. But it was certainly something that was mentioned from time to time, and certainly the

investment bankers would always mention it because of course they can help you with that for a fee.

Hughes: What, in your mind, is the actual reason or reasons for the takeover?

Gower: As opposed to the avoidance of the negative with the takeover, there was— [We thought:] Hmm, okay, now if we end up not being able to have the revenue growth that was projected when we thought we had two more products than we ended up having, and t-PA being half the size we thought it would be, you could afford to put 'X' into research and not have Wall Street choke. But if you put 'Y', which is a number three times that large in, which is what we'll need to get to the next things, whatever they are, that would probably be a huge problem, and maybe we're better off teaming up with someone else who's got a lot of money, but hasn't got a lot of productivity in research. There were various iterations of that in terms of thought. One of them was, and this is something that I did mostly with Bob, although I kept Kirk informed—Bob was supposed to be doing the strategic stuff—to look for a variant of what we did on the product-licensing strategy, look for a mostly European partner with whom we could merge and maintain pretty much control of what we did. And so Bob and I, with Lehman Brothers, were tromping around Europe for a good year before any of the stuff to do with Roche ever started up, and talking with more medium size companies, without naming names, and looking at opportunities where it would have been, even though we were younger, a little bit more of a merger of equals because they didn't have a position in the States or a position in the States that was strong enough, so on and so forth. Near the end of that process, some other factors came into play, some of which were objective, some of which were subjective, that I think basically shifted that into, well, let's look for somebody bigger than that. It became obvious that doing that, while a great solution for the longer term, was probably not going to cover the delta between what we could spend if we were on our own with the product pipeline that was then in place, and what we could if we were underneath the umbrella of a larger company. That's objective. Subjectively, I think the Bob and Kirk battle was beginning to tire everyone, certainly me, but I didn't make those decisions. But I think the most important people it was tiring at that point were Bob, Kirk, and Tom.

Hughes: A critical threesome.

Gower: You got it. And its amazing how attractive under those circumstances something that might not have been as of attractive a year and a half earlier all of a sudden seems. Well, this is an easy way out of this problem, we thought. [laughs]. If Bob can declare victory and Genentech is kept intact, which amazingly happened in the way that deal was structured, surprising a lot of us, even those of us that did the deal. I used to kid Bob and say, "What are you talking about it's not a merger? Of course, it's an acquisition-merger. You're nuts!" "No, no, no, its not—we still have our independence…" "Bob, they own sixty-percent of us. What the hell are you talking about?" But it turned out more or less that way

i. e. [Genentech surviving as a more-or-less independent entity], and that's great. That was in part due to the way Bob thought; in part due to}\some very clever structuring on the part of Fred Frank, vice chairman of Lehman Brothers, the investment bank. I would say in biggest part it was the realization of Jurgen Drews at Roche that if he just melded Genentech into the operating organization at Roche, he would destroy what he was buying.

Hughes: And you could convince him of that?

Gower: I think he convinced himself. And so there were a combination of circumstances that really made that merger unusual, and I think it turned out to be a very smart move. All I am saying is, at the time that it began to evolve, and before we knew anything about the details of what Roche or Drews thought, some of the personal issues were beginning to make it a more palatable idea as well. It also happened to be convenient to get at some of the people answers that we have just been talking about.

Hughes: How much of this was luck—

Gower: Oh, lots!

Hughes: —because what you're saying in a sense is that with these tensions rising between the two at the top, Genentech was more vulnerable.

Gower: Exactly.

Hughes: That's not a good situation to be in when you're trying to find a company that is going to honor the independence of the company that it's acquiring. So why did Roche treat Genentech with respect?

Gower: Oh, two words: Jurgen Drews, who was then the VP of R&D there, and whom I respect a lot. He has turned out to be much more of a thinker than most of the people in pharma in general. If you read some of the articles he was publishing in the late eighties—in *Nature* and the like—in terms of what was happening in the pharmaceutical business—A lot of people in the pharmaceutical business thought he was crazy, but he actually did economic analyses with a guy named Stefan Reiser, who was then I think chief commercial officer at Roche, on how the economics of this business were set—on how big pharma couldn't keep going like this because on average the top ten pharma were able to generate one new chemical entity per year, but they needed three to continue the growth rate, and the like. He more or less forecast well before it happened. Now, everybody would say, well, yes, of course—but not then—that there was going to be a huge merger mania in pharma. Pharma was going to get much more condensed. They were going to turn into much more development and marketing organizations on a global basis, and most of the discovery R&D was going to be done by small fast-moving guys who were willing to take the risks.

Hughes: Yes, look what's happened.

Gower: Exactly. Drews couldn't have been righter, and the nice thing is, it's in print, and you can look back at what he said at the time. He's been quoted immensely, plus he wrote a book, the original was in German, but its been published since in English, which has been cited for most of the decade now in books about the pharmaceutical industry, even recent ones negative on the pharmaceutical industry, published in the last six months about why do drugs cost so much.

[End Tape 5, Side B] ##
[Begin Tape 6, Side A]

Gower Drews felt that one of the problems that Roche had had since benzodiazepines, Valium, Librium, coming up with important new things was that it was very difficult with a global, decentralized organization to get as much productivity out of research, and that groups like Genentech, which had new technology, which was much more coherently focused at it, et cetera, that it was easier. I think that that's true. His point, in terms of how Genentech should be rolled in to Roche, was that if we just made this part of the existing organization and research, which was not producing much, we'd destroy what we bought, so why buy it?

Hughes: I was wondering how Genentech culture would be handled.

Gower: Drews felt that it was extraordinarily important, and in fact he went so far as to decree, and he was *not* a popular guy at a good chunk of Roche, that below pretty much executive level at Basel, no one could visit Genentech without getting his written permission. The guys in Nutley, New Jersey [at a U.S. branch of Roche] hated this. Then he went on later to pretty much rip apart the whole research organization and put it back together again. Because no matter what they thought of themselves, they hadn't invented a drug! Look at Roche's product flow now and where it's coming from: it's coming from these guys. And so Drews was a very, very bright guy, but I am almost totally convinced that if it hadn't of been the fact that Roche corporately needed an infusion of products, knew how to do M and A [merger and acquisition] activity, had bought companies, had a brilliant financial guy, whose name is Henry B. Meier. For many years, many of us had said Roche is a bank that happens to own a pharmaceutical company, because all the money they made was from Meier's approach to things. He bought Syntex for free, because he figured out how in the Swiss banking rules they could take advantage of a corporation that was incorporated in Costa Rica. Genius, financial genius. But they had a way to do it and a guy in Meier, that it was done at his behest, and who was pushing for it, that really felt that the benefit of what they were getting was best achieved if they left as much as they could of the culture and the motivation of the people there intact. Man, is that unusual for a company, even to this day. So I think that it was lucky, yes, but it's turned out to be fortunate for both organizations.

Hughes: Say more about Fred Frank's role.

Gower: Well, he was key. Fred is an investment banker; he's the vice chairman of Lehman Brothers. He's incredibly well-known in this business. He's done a lot of the mergers in major pharma, has done a lot of the ones in biopharma. He's been a little bit of everybody's banker over the years, and he knows everybody. He did the Bristol-Myers-Squib merger—tons of this stuff. Fred's role in the Genentech-Roche merger was in structuring something and helping sell it, financially, to both sides because he was actually willing to think and apply new structures. Okay, Bob, you want it to be independent and, Jurgen, you want it Genentech's science to have these elements of independence. How the hell do we do this and also make it something that you guys get the economic benefit out of and so on and so forth? That's not easy. That's not a traditional investment banker role, believe me. Most aren't *that* creative, but Fred really worked at this. From an implementation standpoint, it wasn't his idea. That came out of Bob and Kirk and Tom. And it certainly wasn't his idea to tell Jurgen what to think; Jurgen already thought that. That part was luck. Back to more general strategy, which I firmly believe in, but eighty percent of everything is implementation. If he hadn't put together a structure that made sense to the individual shareholders and to the financial market, it still wouldn't have happened. So Fred was very important in that, and a lot of that was really individually convincing the then chairman of Roche and Bob that on individual points that came up: no, no, no, this makes sense, and this works because of this that and the other, or to re-jiggle the structure slightly. So from an implementation standpoint he had a lot to do with it.

Hughes: Did he also have a key role in the valuation process?

Gower: Yes*, the* key role.

Hughes: Do you want to say something?

Gower: No.

Hughes: [laughs] Why not?

Gower: Well, let me go back to what a prior era's Warren Buffet said, Bernard Baruch, back in the thirties. When asked [for a stock-market prediction] he said, "Over time, the markets will vary." [laughter] It's a very famous quote, but only for those of us that care about financial stuff. You just can't say much more than that about Wall Street valuations, et cetera. But certainly it is a touchstone emotionally, with the CEOs especially, but in general with the employees of every company that's affected by it. No matter what you do, most people are going to dislike it, I think, and have to have it sold to them by their respective CEOs, no matter which side of the transaction they're on. It's actually quite amusing. So Fred had a lot to do with the structuring so that everybody at least

on paper got to have their cake and eat it, too. The existing shareholders got bought out at a differential rate than the cash left in the treasury for use in developing the products. That was much nearer the market price, the price that went to buy out existing shareholders and convert to Roche shares, what was much more of a premium to the stock price at the time, and the blended average price was somewhere in the middle. And that's not either unethical, illegal, or in fact hard to figure out if you read the statements. But it's the sort of thing that you've got to do in playing to all those markets to make it worthwhile. You end up with a valuation that is in the short term palatable, and that the Street will vote in favor of, and that's art, not science. [laughs] It's emotion that creates valuation, not hard facts.

Hughes: What products were targeted after t-PA, once it was clear that the Roche deal was going to go through? Who was then making those decisions?

Gower: Well, after the merger, in the course of about a year, a number of things happened. Art became head of research and began to make those decisions. Bob moved up to chairman, got out of the way of the ongoing management of the business. So it was just one of them that was doing this, and that in and of itself was better. So I would give Art most of the credit in terms of what was chosen—Let me scratch that, I give him all the credit, although there's some people working for him that I happen to know and respect that had a lot to do with it, too. But in terms of top management, and certainly the folk we've talked about, Art was the only one that made any difference. He picked the things because somebody had to. You couldn't just have this endless process of deciding what to do. Once he was in charge, he decided with a lot of people's input, okay, we're going to do this; we're not going to do that. Oh yes, once again they voted on not to do vaccines, by the way. [laughs]

Hughes: Really, that did come up?

Gower: Sure. It was the HIV vaccine then, which is much more important to me than foot and mouth disease vaccine—if it worked. But Art said, "No, we're going to do it for a while, but basically I want to— Don [Francis], I love you dearly, but I don't think this is going to work." And he called that right. So he charged the guy that was then in charge of business development who worked for Gary Lyons who worked for me. (Both of us were gone over the first part of the nineties.) Nick Simon was here. Go spin out the AIDS vaccine program; turn it into a separate corporation [VaxGen], et cetera. So they found some way of gaining value on those things they invested money in but didn't really want to make part of the product feature. And the things that got elevated—well, fanning is the wrong word—but not moving with the alacrity that you'd ideally like, were things like anti-HR2 (Herceptin) and the anti-IGE program; those I think were the two primary things. Rituxan, which was another antibody, did not come along until a little bit later while I was gone. It was more optimistic on their side in terms of them understanding the technology, being one of the few people in

the world to make the stuff, and deciding it had made a great fit together with the other two in terms of the direction they were going in. So it worked right and it worked for them, but I was certainly part of that decision. So it started almost immediately. It's just that the culmination of that in our business, drugs, takes several years to play out no matter when the decisions are made. You've got a fair path to get to convince the FDA that it makes sense. Art moved with a pretty straightforward decision-making process after he was put in charge of research, well before he was made president; after the Roche merger, he just got on with life. That's what happened.

One thing that was decided slightly before the Roche deal, and it also turned out okay. Pulmozyme, which is important to cystic fibrosis patients, wasn't a huge drug but it helped. It was yet another drug, and Art had a lot to do with that, too.

Hughes: I read that there was a lawsuit or two from the shareholders.

Gower: I think there were two. There was one when I was there; I'm not sure the timing of the other one.

Hughes: What about the put and call, the complicated scheme about the shares?

Gower: Oh, the second Roche deal.

Hughes: Yes.

Gower: That was more Fred Frank's structure. Well, that was the start of Kirk's demise. So what would that be, '93, '94, somewhere in there. I was gone by then; we had started up Tularik by then. So Dave [Goeddel] was gone, too.

Hughes: Yes, you left in '91. I would rather get the story from someone who lived through the second Roche deal.

Gower: I couldn't agree more.

Hughes: [laughs] What would you like to say in greater detail about the Roche acquisition? Have we covered it adequately?

Gower: Well, I think the only thing that has gone unsaid. I'm not sure it's the most important thing to say, but it's the only thing that probably is worth a footnote: in and of the circumstance with Bob and Kirk, I'm not really sure we needed the merger with Roche. Financially, it wasn't a necessity; we were generating cash. Aside from aborting a negative, like takeover, could we have made the same decisions if we just got on with the management side of it? That was the problem. And I'm not saying it would have been better.

Hughes: Art was still there.

Gower: Yes, the same cast of characters ended up making the same thing out of what they would have done anyway. You never know, because you can't replay history, and that's why I call it a footnote. I don't know. I waxed hot and cold at the time of whether the merger made any sense and finally decided that it was worth so much money to me individually, that what the hell? As I told Bob Swanson, I'd been figuratively selling Genentech for a decade; why not do it literally? But I think it's at least worth a mention, if nobody else has, because I can think of only one other person that would say it. It was the other person besides me that was doing the structuring.

Hughes: Nobody else has said it to me.

Gower: Well, only John McLaughlin could say that, who became general counsel, in '88, I think, and is now president for Corgentech [Anesiva], and so on. But we both kind of in the back of our mind felt that this could have just as easily gone another way. You can't do that experiment, so you can't say it would have been better. But it's at least worth noting that by any classical standard, like running out of money and the like, Genentech didn't have to do this. It was a choice. It wasn't a hostile takeover, and we weren't running out of money; it was a matter of what's the best way to deal with the future. That's just my opinion.

Hughes: Yes, well it's an interesting thought, to say the least.

Gower: What other things haven't we talked about?

Hughes: A lot of things. One of them is: did it come from Roche that Raab was to be CEO? That's been stated as a criterion for the deal to go through.

Gower: Hmm…Criterion for the deal to go through, I think that's too strong. Were there signals that that would make Roche more comfortable? Yes. So maybe it's the same thing. If there were to have been a resolution to the management issues prior to Roche coming up, and it had been pushed strongly back by Kirk or Bob or Tom, I'm not sure it would have gotten in the way of the deal. I don't think Roche really cared. I mean think about it. They weren't hiring *that*.

Hughes: They were hiring much more than that.

Gower: Yes. *They—actually—knew—what—they—were—buying*. [Stated with a pause between words.] It may sound strange that I say it that way. But if you look at most mergers that don't work, a lot of times it's because there's not a clear explanation of what you're really trying to get out of it. Roche was very clearly trying to get to products.

Hughes: Yes, but at that stage, they didn't know *what* products. There's a difference between saying, "This is a company that has produced; it's got a culture that we think will continue to produce; that's what we're buying," as opposed to saying,

"Well, we see Rituxan; we see this specific product; we see that specific product."

Gower: Well, they couldn't see Rituxan.

Hughes: Okay, bad example. Roche must have been able to see… Well, maybe they couldn't?

Gower: No, they couldn't. I mean you would have to ask Jurgen Drews to get the actual answer to that question, because he would be literally the only one that would know, because what the other guys at Roche thought was what he told them. So it literally is one-stop shopping for that. From what was on the potential products list that we presented to them, and that Drews went over, since none of them were in the clinic, you couldn't say that he saw a product. He saw that there were a lot of quality ideas that he happened to buy into. I'm sure if Art hadn't gone ahead and made decisions, Drews would have found some way to get some decisions made so that we could get ahead with some of the other ideas. But there were multiple opportunities, and all very, very solid product opportunities. But it clearly wasn't tangible, because it wasn't like we had another program coming down the pathway that was only two or three years off, that was visible. That's not true.

Hughes: Well, it reinforces your point that Roche was buying a company, with everything that that meant.

Gower: They were buying a group of people with demonstrated capability to take this new science and produce products out of it on an ongoing basis. That was that, and I think that is almost what Drews would say.

Hughes: Is that the way mergers now occur—you are buying a company in the widest sense? Or has it become, no, you are buying a company because it has products one, two, three?

Gower: Well, in the aftermath of the Roche-Genentech merger in what was called the sixty-forty solution, which is the structure of the deal where the acquirer owns sixty percent but couldn't go past that, yada, yada. I mean, it was this complex structure that Fred put together, that actually worked. There were a number of deals done, including Immunex way back when. (Amgen finally bought American Home Products out of that.) Genetics Institute went that way, and is now part of Wyeth, et cetera. I would say these days it's more product oriented, but that's because of where pharma is today as versus where they were then. Today they don't need more potential; they need more products. There's not a pharma company out there where what Jurgen wrote in the late eighties hasn't come true. Now everybody says it. My god, Merck holds cocktail parties at the bio meeting just to make sure they're thought of as partners. It would have been an anathema ten years ago inside Merck to have a cocktail party to promote

themselves as a good biotech partner. Merck virtually invented the concept of not-invented-here. But not anymore! As they said to me once in the last six months, "It's not your grandfather's Merck." I think the world has changed. Pharma circumstances have changed, so mergers right now are a little different. But in the aftermath of the Roche-Genentech merger, it changed a lot of things, and a lot of people copied, followed, whatever you want to say, that particular approach to it and even the formulas to how the deal was being done. That probably was imitation or copying, as opposed to the Amgen generally following the same approach we did, which was more the spirit of it, but not *exactly* implementing it in *exactly* the same way. Because a lot of people just ripped off that structure and duplicated it.

Hughes: You would give Fred Frank credit for the merger structure?

Gower: Not just me, the whole industry would and has. He was at the biotech CEOs meeting which then was run by Kleiner-Perkins and Ernst and Young, and is now by a lot of groups. But it still happens, which is the only time each year biotech CEOs get together with no real outsiders so you do not have to be "on". They gave him their man of the year [award]. I forget exactly what Brook Byers called it, but it's something like, "The Man for All Seasons and All Times in Biotech. The Guy that Walks on Water." We were out by a pool at the Ritz-Carleton at Laguna Niguel, and as only Fred could do, of course suited as a banker, proceeded to pick up on that line and attempt to walk across the pool to accept the award. [laughter] He ended up treading through the water in full suit and tie, and everybody just cracked up.

But the merger was a transforming event in biotech in more than just the financial piece for one company. It basically marked a sea change in pharma-biotech's relationship to each other. For the first time, it was past the point of that early breakfast meeting that I mentioned with the then-chairman of Pfizer that Bob and I had had in the early eighties where people were saying, "Well, I'm not even sure I believe in this biotech stuff." Although this was simply the first of many events to follow, that point around 1990 marked a shift. If you look backward at the products going into the FDA, there was a shift from most of them coming from pharma to most of them coming from biotech, and that's especially true today. So the Roche-Genentech merger was symbolic, it was important in showing *how* to get it done. It was important in reinforcing that pharma was probably not capable on its own of coming up with enough products for all sorts of things, and that small companies which are more geared to focus on new technology and science and to put it in place is not a crazy way to go at this. It meant a lot of things to a lot of people, so that's why Fred Frank was fairly widely lauded at the time, even by people that got no financial gain whatsoever out of the merger and didn't work for Genentech or Roche.

Hughes: Well, should we stop there?

Gower: I'd be glad to.

Hughes: Well, I thank you. It's been a real pleasure.

Gower: Well, it's been a pleasure talking to you.

[End Tape 6, Side A] ##
[End of Interview]

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James M. Gower is Chief Executive Officer and Chairman of the Board of Rigel Pharmaceuticals, Inc. From 1992 to March 1996 Mr. Gower was president and chief executive officer of Tularik, Inc., a biotechnology company developing small-molecule drugs regulating gene expression, and served as senior vice president at Genentech. At Tularik, Mr. Gower was involved in the development of the company from its inception until 1996 when it had approximately 100 employees, five corporate partnerships, and a positive cash flow from operations. During his ten years at Genentech, Mr. Gower had a lead responsibility for business development and sales and marketing functions. He established and managed Genentech's foreign operations in Canada and Japan and served as president of Genentech Development Corporation. As part of his responsibilities, he was involved in raising over $400,000,000 from corporate partners and investors in Genentech Developments Limited R&D partnerships. During his tenure, three pharmaceutical products were launched, achieving sales of over $500,000,000 by his departure in 1990. He previously held various positions with American Hospital Supply Corporation. In addition to his role at Rigel, Mr. Gower serves as director of the board of Cell Genesys, Inc. He holds an MBA from the University of Tennessee.

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Sally Smith Hughes is a historian of science at ROHO whose research focuses on the recent history of bioscience. She began work in oral history at the Bancroft Library in 1978 and joined ROHO in 1980. She has conducted interviews for over 200 oral histories, whose subjects range from the AIDS epidemic to medical physics. Her focus for the past decade has been on the biotechnology industry in northern California. She is the author of *The Virus: A History of the Concept* and an article in *Isis*, the journal of the History of Science Society, on the commercialization of molecular biology.