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Developing Products that Save Lives [Entire Talk]

Richard Scheller, *Genentech*

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As Genentech's Executive Vice President of Research and Early Development, Richard Scheller leads scientists discovering medicines that will significantly impact the lives of patients. In this candid interview, he describes the challenges of his industry, and outlines the required steps for developing products in a heavily regulated environment. Scheller also shares some personal learning curves faced when he elected to leave academic life for a new role in a commercial enterprise.

Transcript

It is my very special privilege to welcome our guest today. Richard Scheller is the head of R&Dat Genentech. But I have known him for a very long time although he doesn't actually remember it. He started at Stanford as a faculty member in 1982 and in the Neuroscience Department and then Biology, and that was the year that I was a first year PhD student over there. So, I took classes from him. And it's absolutely amazing to see the trajectory of his career. He spent 19 years at Stanford and then went to Genentech. He's been there ten years and he's got some incredible insights about the difference between research and academia and in the industry and we're going to dive right in. So, welcome. Thank you very much for joining us.

Thank you. Pleasure to be here. And maybe you could tell us a little bit about your story and about moving from academia, about what would motivate you. Tell us a little bit about how that happened. OK. I'm going to stand up if that's OK. Thanks for having me. I was a professor here for 19 years. I was a successful, member of the National Academy. I was a Hughes investigator so I had plenty of money.

Things were going well. But the research that I was doing had gone through a phase where the knowledge had just exploded over the last decade and the rate of learning started to sort of plateau a little bit. So I just took stock in where I was headed with the rest of my career and thought that I had to do one of a couple of things. Find some new technology to increase that rate of learning again or switch my field to a little bit something different where I felt was sort of prime for that tremendous gain of knowledge again or maybe just do something different. So my wife, who's on faculty here, and I thought, "Should we move to Boston?" I get to go to Boston and have a bunch of nice colleagues there and then have labs there. But it really wouldn't be very different than here, given that we didn't have any problems here. We loved it here. So I thought if I was going to do something different and move somewhere, since being a professor here is terrific, that I should really move somewhere where it would be quite different. So I thought then what would that be? It seemed to me then that we have done and when I say "we" in this case, I mean, the life science endeavor, not my lab. So everything funded by NIH for years and years.

That sort of done what we've promised the society that we would do, which is learn enough about the way cells work and the way tissues work and enough about molecular biology. So that we can actually think about disease in very, very mechanistic terms which is the way I like to think. And wouldn't it be interesting to try and apply my biological insights to disease? So I was fortunate enough then to have somebody. David Botstein was in the Genetics Department at the time, had work with Genentech. He kind of heard I was looking around at different things. He introduced me to the CEO of Genentech at the time, Art Levinson. Art was a scientist, started off in a lab at Genentech, became the CEO. And I thought, "Wow, you know, if I'm going to actually have a boss," which was kind of a novel concept to a faculty member, "if I'm going to have a boss, it

should be someone who's a scientist who can actually understand logic and things like that." Someone that I could talk to. So it seemed like a terrific challenge, a terrific opportunity and that it would be really, really different from what I was doing day to day at Stanford. So, I remember over the Christmas holiday ten years ago thinking, "Should I do this? Should I do this?" Walking into the lab and thinking, "So nice here.

My God, I have tenure. Should I do this? What if they fire me?" I could get fired if I go. These are all kind of novel notions to think about but it just seem like a terrific opportunity and I took the plunge and I have to say for me, personally, it was the right thing to do. My learning curve picked up again immediately learning all about kinds of new science, about cancer biology. I didn't really know that. I knew about cell biology but I didn't know specifically about cancer or immunology. I knew absolutely nothing about business. I was on the executive committee of the company. I had to find out what EPS stood for. Really, the executive committee meetings were just learning all about business, all about drug development.

How do you develop a drug? I never thought of that before. So it was just absolutely fascinating. I have to say I give the company a lot of credit because, basically, I think it has paid off for them. But it took me two years before I had any idea what I was even doing in business. I mean, I knew about science but it really was a steep learning curve but not something that happens overnight. So for me, personally, I would say I took the leap because I wanted to do something different and I felt it was the right time to become basically a human experimental biologist, which is what we do all in the context of disease, of course. So I want to build on something you just said. Yup. Because you said you were curious about what it felt like have a boss. Yup.

But you also now have 2,000 people working for you. How did you learn how to be a boss with that many people? I mean that's going to be a huge challenge to manage a team that size. Well, that was part of the two years of learning and that was probably the biggest part. One of the huge differences is, I found that in business, you actually get feedback on how you're doing. I'm sorry, unlike here, at least when I was a professor. Yeah, you might see a chairman in the hall every year or so. But you basically did your own thing and then, nobody really provided you as much feedback. So one of the things that I did there was... Someone said to me, "You should meet the head of HR." And I said, "What does that stand for?" Honestly, I have no idea what that stood for. He said, "Human Resources." I said, "Oh, Human Resources." That kind of sounded to me like they must hire the people.

So then someone explained to me what HR is and they do all sorts of things and so on, so I learned. But one of the things that the Executive Committee of Genentech at the time decided to do is to collect 360-feedback from our peers and folks that work for us and sort of tell us how we're doing. So this was a really novel experience for me. My first 360-feedback, let me see if I can remember. They said I was aloof, arrogant and dismissive. And I said, "Of course, I am. How do you think I survived as a scientist?" It was a competitive arena. But they said, "Well, you know BS. It's probably not going to work here. So what we'd like you to do is then to go discuss your 360 feedback with your reports and one level down, your directors." So I said, "Wow.

OK, we'll go do that." So I went into the room with these people and as a fact, I knew that, yes, most of these people said that I was those things. I didn't know anyone specifically who said it. Of course, it was anonymous. But I said, "Well, gee, people say I'm aloof, dismissive and arrogant and I can't understand this. I mean, my parents said that. My wife says that, my colleges at Stanford say that. You say that. I cannot figure out how you're all wrong in the same way." So I basically found that you need to be a much better listener. You need to really, really respect folks and their opinions. But it is very, it is different in industry compared to being here.

I think part of the reason that people found me quite brash was the fact that here, when I said something, nobody actually did what I said. Hopefully, they at least marginally considered it, but then they would go, "No, really?" I mean, post docs, students and then they go do really what they wanted to do, which was fine. So I took that attitude to Genentech and actually found very quickly that-well, I didn't really want the atmosphere of the company to be that way-but it is just different and it is somewhat more hierarchical and that people actually do what you say. So you have to be really careful with what you say because folks are going to take it incredibly seriously. So it's just a million little things like that you learn over time about how it's different in the industry versus academia. But the reason I say that it took me two years before I felt as though I was coming to a place where I really knew what I was doing and could be sort of ultimately productive. So there's no really one thing that I can say that I learned. But I hope I gave you kind of a couple of examples there of what I would say would be a list of a thousand things, if I wrote them all down. So maybe you could tell us a little bit about what your responsibilities are. I mean, head of R&Dof a large biotech company, it sounds very impressive.

But maybe there, you could give us an insight of what your real responsibilities are. Yes, so I'm in charge of discovering medicines that will make a real difference in people's lives. So, as you may know Genentech is now an incorporated company in the United States but 100 percent owned by a large Swiss drug company called Roche. But our group is completely independent and our job is to discover medicines that make a difference. We don't make any generic drugs. We don't make any copies of other drugs. Innovation is our... We're going to live or die based on innovation. We also believe very strongly in the view of personalized medicine. That is, making medicines that are tailored to individuals.

The Roche group owns two businesses: a pharmaceutical business and a diagnostic business. So, very large, I don't know, maybe fourth, fifth largest pharmaceutical company in the world and the largest diagnostic company in the world. So the idea is to make medicines that really, really deliver benefit-tangible, terrific benefit-for people. So if we make a medicine for somebody with cancer, we have to show that they actually live longer when they take the medicine, for example. So I oversee research. So our research group is about 1,300 folks. We have about 150 of the people who are post docs. Now, why would we have a post-doc program? People come through. They come from all over the world. They stay for four five years.

They bring in new techniques and ideas. They're not cynical yet. They work at night and in the weekends and it just energizes the place. Then we have scientists at various levels. And the job of the scientist is two-fold, to do basic science. We'd like to give each of our scientists somewhere, some what we call discretionary time. Maybe it's somewhere between 10 and 30 percent of their time, so it depends on the individuals. Some people are, frankly, it's a 100 percent but that's a different topic. And with their discretionary time, they're supposed to just do interesting things. Do whatever you want; make a discovery, publish a paper.

We published 20 papers in science, nature and cell last year; hundreds of papers overall from the company. But the other real tangible deliverable of the scientist is to come up with a medicine and move that medicine into what we call early development. And in early development, the compound goes through various further stages of testing to make sure that it's safe. We do all the work to file in I&D That's a new drug application with the FDA and we file the I&Dand then we do the clinical studies Phase I and Phase II. In Phase I, you usually just treat patients. Then, make sure that the drug is safe. You start at a very, very low dose. I mean, imagine, putting something into a human that's never been in a human before. Slowly, escalate the dose.

It depends on the disease. Sometimes it will be in patients with the disease, sometimes not. But then, usually in Phase II, you do a relatively small number of patients but enough patients so that you have statistical power to see that you're making a difference in the disease. And what we then do would be, if their Phase II trial works, to hand the medicine to them, the Global Development Group, to do the final clinical testing. And the final clinical testing would then be done in 80 countries around the world. It's a logistical absolute nightmare. It's done in many, many more patients so that the statistical power increases dramatically. And then, work with the regulatory authorities to get permission, if you will-so the FDA, in case of the United States-permission to market the drug. So my job is to deliver molecules that we say have gone through proof of concept. We believe that they work.

We have the chemical entity. We know that it can be manufactured and to hand this to the Global Group where there's a lot of science involved but there's a huge amount of logistics and regulatory involvement. And that's when the commercial people get involved and so on. Frankly, I'm less interested in that. I then go back and try to discover a new medicine and show that it works. So, can I chime in here because I think it would be fascinating to everyone to know how many of these you generate, how long it takes and how many actually are successful. I mean, this is a very complex process and how many sort of pop out at the other end as successful? Yes, well, this is... That's a tough business. So, I would say, from the concept of "maybe this molecule would work in this disease" to actually marketing the drug, well, it depends. If it went incredibly fast it could be ten years.

It's more like 15 years and the average cost is about $1.5 billion to get it to the market. Now the $1.5 billion includes the failures. So that's taken into account. So how many make it? That varies from company to company. I would say probably on the average 10 percent make it. For us, it's probably more like 25 percent. But I think the industry is going to do much, much better in the next decade. And the reason is that there's been an explosion in knowledge about biology. What I think was happening in the industry in the '80s and the '90s, there were a bunch of successes. Drug companies-Merck, Pfizer, Roche-they were making tons of money.

And then, they're saying "But we've got to stay a growth company. We need to grow." So they gave a lot of money to the heads of R&D But frankly, they weren't very good targets. But what is the head of R&Dsupposed to do? Say, "I don't know what to do. They aren't very good target. Here, take the money back"? No, of course not. They spent the money on lousy targets. But during that time, there was a tremendous revolution in the understanding of biology that was taking place which, as I said, is partially why I moved to industry. And I think that now there are incredible targets that we work on. Think about cancer.

We take the cancer, we take the tumor, we sequence the DNA of the tumor. When we sequence the DNA of the normal tissue, we find out what genes are mutated, what genes are actually causing the cell to be a cancer cell. And then, it target those. Is that going to work? Yes, it's going to work. But they are working. You know they work. But that is just terrific sort of pre-clinical validation. Those are the kinds of things that you want to work on versus not knowing what to work on. So, it's an expensive and difficult process. Also, the industry is facing a lot of head wins from various countries including our country, on being willing to pay for prescription drugs.

Some of our drugs are extremely expensive. If we make a drug for a certain cancer and their 10,000 patients per year, it's not unusual to charge around $50,000, $60,000 a year for the drug, which we have to in order to basically re-coop the investment. But, look, if you're going to live longer we think it's delivering value. So there's a lot of pressure on payers and a lot of pressure in Europe, as well. I voted for Obama that is charging Genentech $550 million this year to pay for Obama care. Now, where do we get $550 million? We fired $550 million worth of people. Where else are we going to get the money? So now they don't have jobs or health care. But these are the kinds of things that all companies are going through. There been thousands and thousands of people laid off from the pharmaceutical industry because of the pressure on pricing and the rebates that people are asking for. I think this is what happens during tough economic times but there's a price that's paid for that in our ability to develop new drugs.

So, let me drill down on this question of small markets. Because, I know there's a big interest in personalized medicine which is like the smallest market you could get, right? I mean, it's just for the one person, it's very personalized. How interested is Genentech in this and what are the consequences both for the market, for the cost, for the consumer? As I said we've staked the whole company on the idea of personalized medicine but that doesn't mean it's for one individual. That, of course, wouldn't work. So, for instance, we market a drug called Herceptin, which is for about 20 percent of patients, women with breast cancer, and this drug is extremely effective in this 20 percent of women. And there's a test to know whether the gene that is the target of this drug is amplified. So, in most of your cells, you have two copies of this gene and 20 percent of women with breast cancer, you have about a thousand copies of this gene and the drug is extremely effective. So 20 percent of breast cancer, I forget what the worldwide sale of Herceptin was last year. You can look it up but it's something like $3 billion. So that's not so bad.

But, you're right. As we get down the smaller and smaller populations, other market becomes smaller and smaller. But two things happen. First of all, our failure rate will go down. We understand more about the disease, more about the molecule, more about the target. So the drug, we believe that the drug will more... Our clinical trials would be more successful, number one. Number two, if the drug really works, you know what patients to treat, you drive penetration. So, almost every woman in the United States that has HER2 positive breast cancer gets Herceptin and it would be sheer malpractice not to prescribe Herceptin. So, we have a sales force but-boy, I know I'm getting real trouble with this talk-we have a sales force but all doctors would use it anyway.

Because they know that it works really well and this is the standard of care. So we expect that there'll be a higher success rate, deeper penetration into the markets with the personalized health care approach. We will also market the test as part of the Roche group which will help with earnings, although the diagnostic business is very different than the pharmaceutical business in terms of margin and so on. So, you're talking about failure a second ago. Yeah, yeah. And let's talk about that a little bit. Because we all know that if you're going to take some risks and some big risk, you're going to have a higher chance of failure. But these risks if they work out, you can have some really big hits. So, how do you encourage that type of innovation and risk taking in the organization if people know that, "Boy, if I fail, this is going to be an incredibly expensive failure."? So there must be a lot of tension between that or how do you walk that line - trying to encourage risk-taking and innovation and not wanting to have some big failures. Yeah.

Well, we just have to accept that we're going to have big failures. So we have a portfolio balance portfolio approach. So, for instance, in the Phase III, portfolio now has 13 new molecular entities. So with that, that's a new compound. I say 13 because there are probably 50 clinical studies going on. Sometimes the molecules are tested in more than one type of cancer, for example, and those are separate studies. So 13 new molecular entities, each one, by that stage, has a commercial value associated with it. That's also getting better but those are usually wrong. I mean, the drug that we sell a lytic for dissolving blood clot was supposed to be a several billion dollar drug and it sells $200 million a year. And a drug for non-Hodgkin's lymphoma was supposed to be a couple of hundred million a year and last year, it was the largest selling drug in the Roche group and sold $6 billion.

So it's just the opposite of what the commercial prediction's were. But that's better now than it was 10 years ago. So we have a commercial value associated with each molecule. And then, we have associated with that a probability of technical success, a probability that the molecule will work in Phase III. And we take that all the way back, even to the portfolio that I managed in Phase I, where we have a probability of technical success of the molecule getting to the market. So what's the probability it will make it through Phase I, probability through Phase II, Phase III, through regulatory. Obviously, as a molecule moves through the pipeline, the probability goes up as it passes one hurdle, and the next hurdle and the hurdle. So, we have a portfolio with known value for each molecule and the probability of the molecules working. And then, we balance the portfolio with more risky projects and projects that we feel are close to a slam dunk, if there ever is such a thing in our business, and manage the portfolio that way. So I know that there are a lot of drug companies that outsource their R&D

They have lots of little smaller drug companies that are trying lots of risky things and when they get down the pipeline, they license it or buy it or buy the company. Do you guys do that or do you ever outsourced R&D I wouldn't say. Well, the short

answer is, sort of. So, we're very good at R&Dat Genentech. We're very proud of that. I think that a lot of companies have lost their way in terms of their research and development and frankly don't have the quality of scientist that we have. I guess I can say that if I don't mention any particular company. So they have to look outside for their molecules. Now, if you're going to start a biotech company, you can get some scientist together. You can do some experiments.

You can maybe raise enough money to get a molecule into the clinic. But remember as you start doing the later stage experiments, these experiments cost hundreds and millions of dollars and it's unlikely that any small company... I would say it's not unlikely, it is impossible nowadays that any small biotech company would be able to raise enough money to do its own large Phase III clinical trials. So the companies have to partner with larger pharmaceutical companies which have the resources to do that. So, while we have 1,300 scientist at Genentech-that doesn't include the clinical groups and so on-however many scientists we have, we will always be a small part of the overall life science industry. And I have a business development group that reports to me, just 25 people. Many have PhDs and MBA; some have MDs, PhDs and MBAs. I'm under educated compared to some of these people. And they have the world divided up into territories and we're constantly looking to in-license innovation that comes from outside of Genentech. So we're very, very conscious that we don't have all the good ideas.

We don't invent all the good things. Hopefully, we're somewhat less dependent on it than some of the other pharmaceutical companies who's R&Dmay not be quite as good, where they, as you said, almost solely depend now on in-licensing. Some of the companies have so much money and are getting so desperate because of the drugs coming off of patents. When a drug comes off of a patent and becomes generic, if it's a simple chemical, not a protein antibody, the generic companies move in and basically, the innovator price falls by usually about ten-fold in six months. And there's huge, huge patent expiries coming in the industry. So people are quite desperate right now. So I would say a lot, but they made a ton of money off of these molecules over the last decade. So now going to the small company and say, "Look, we don't to license it. How much do you want? We'll buy you." And, yeah, that can be a very lucrative model for a start-up biotechs, if you can bring a molecule into the clinic and interest a large pharmaceutical company in the molecule and start with, let say, $20 or $50 million of capital and sell the company five or seven years later for half a billion dollars. So that's not bad.

You have to be successful to do that. Yeah, very interesting. Well, let's go back to academics for a little bit and the comparison between academic and commercial drug development. When you're in academic, your lifeblood is grants and you're getting grants mostly from the government but probably also from some drug companies as well. And such a small percentage of people get them. Let's have a deficiency of that versus being in a company where you have a very different model. Do people inside Genentech have to actually compete for money and resources? Is there any parallel inside a company to what people might be familiar within an academic setting? Yeah, so just think of me as the NIH. Yeah. So, there's never enough money to do all of the ideas that you'd like to do. So even though we have a very nice budget, we do have things that we can't do.

There's never enough post docs for folks. But we fund each of the.. Each typical scientist, entering scientist, at Genentech will have a post doc and two technicians. And we ask our scientists to-well, they don't teach, they don't have to raise money by writing grants-we ask our scientist to actually still work in the lab. Whereas, an assistant professor here, at least my experience was some years ago, were very quickly at least in the life science, have teaching and grant writing and going around and giving talks. So it will be very hard to actually stay in the lab very long. So we ask our scientist to really work in the lab. We fund everyone about the same. It's really FTE driven. And as you might become a senior scientist, or go on to be what we call a staff scientist, the laboratories can grow to five or ten people.

But again, people are treated fairly, fairly similarly. Although, it's certainly somewhat dependent on the project that you're working on, if it's particularly hot or important and if there's still something that we could help by money to shorten the timelines, we would review that and understand that. Even at the research stage, each of the translational projects have timelines. We have goals, we have certain expectations that we try and meet on a monthly or yearly basis. So it's somewhat more, it's quite bit more organized than at least my laboratory was, which functioned a lot more on sort of churn. I mean, I meet with people and I'd say let's try and get that done in a couple of weeks or something but the scientists wouldn't come and make a presentation. They have, at the end, a timeline for when we might expect that something would move in to clinical development. But we have to have that again in order to manage a portfolio and manage a flow of molecules through a pipeline. Let me see, I think that we don't waste money, but money doesn't hold back our best ideas at all. And we don't spend a lot of time...

Well, I spend time with the CEO haggling about my budget but none of the 2,000 people who work for me spend very much time worrying about money, really. That's terrific. So I'm going to ask one more question and then I'm going to open it up to the audience so you can spend the time thinking about your provocation questions you want to ask Richard Scheller. So, let's go back to when you were in school. I know the fact you started talking about the fact that you ended up in this position and it took two years to really get up to speed. And a lot of the students here are lucky enough, even when they're getting a technical

education, to get exposure to courses on business related topics, on strategy, on marketing and finance and leadership. What are the things do you wish you have learned when you were in school? What would have been the most valuable things that would have helped you really hit the ground running when you were walking into a really important leadership position? People ask that and I think any time that I would have spent getting an MBA, for example, wouldn't have been worth it. I really think that the reason I was hired is because I was a really, really good scientist and taking-you notice the was-any time away from that would have frankly been a mistake, I think. And the only reason our company will be successful in the future is if the right technical decisions are made. And people don't get that.

It all depends on the science. If we pick the wrong target, if we make the wrong molecule, if we choose the wrong disease, we try and develop it and it doesn't work over and over again, the company is finished. It's all driven by the scientific decisions that are made at the early stages and through development. You can have all... I mean we need the commercial folks. So they're terrific, I love going to the sales meeting and the manufacturing people and the finance folks, that's all absolutely critical. But if the science is wrong, there's no foundation, there's no basis for the company. So I think just becoming the absolute best scientist that I could be in being just so focused on that was actually the best use of my time to be the best head of R&D So, nothing. Nothing different.

So... But the fact... Wait a minute, what you're saying is... I mean, now, seriously. Now, what you're saying though is it was the best of your time and to basically learn it on the job as needed? Yup. Absolutely. As needed when you basically throw yourself and you got just in time knowledge from the people who... Because of those, the scientific decisions, out of the executive committee room, if the scientific decisions weren't right, no basis for the company. That had to be there. Great.

Very terrific point of view. OK, so any questions? Great. Right here. So can you talk a little bit about sort of the balance of how much innovation has gone from the academia versus the commercial sectors? In terms of like when a drug is released, how much of the... is from the actual drug manufacturers versus, say, fundamental discoveries from academia? Richard, will you repeat the question so that others can hear. Sure. To talk a little bit about how much of the balance between the academia and the industry input into a drug. So when a drug is released, who did the work, basically? So it varies drug to drug. I mean some drugs, we discover the target, we make the molecule, we do all the development and the contribution from the academia is pretty much what I would call zero. In cancer, for example now, a lot of targets are found.

Somebody sequences eight years ago, PI3-kinase in finds that it's mutated in 30 percent of breast cancer. We read that in Nature and we say, "Oh, that's probably a good target." But then we do all the work on making the drug and testing it and so on. So that sort of have been, I would say, an immediate to the major discover that's made in the academia but the company does all the work to develop the drug. And then, there are other situations where someone in academia may make a monoclonal antibody and then they may show in a model, of some mouse model, in some disease that this monoclonal antibody seems to help with the disease. They may then license it to Genentech and we would then take it from there, usually into the clinic. So I think it's very rarely the case that, not impossible, but rarely the case that an academic would take a molecule on their own into clinical testing. For instance, to take a monoclonal antibody into humans just to do the process development of getting the molecule, it has to be GMP-made and approved by the FDA and put in bottles and so on before it can go into a... It's $25 million so it's a hard thing for most academics to do it without some kind of industry sponsor. So that's an idea. Right.

Yup. Once you get the molecule working, how do you disseminate that knowledge among 2,000 scientists? What are your knowledge management mechanisms? So the question is once we get the molecule working, or really basically once we do anything, how do we disseminate information? We have a variety of ways. We have a Web, of course, for what we call Genentech Research and Early Development. We post clinical findings there once they're made public. We post publications that are made. Clinical scientists and basic scientists give seminars. We also give a lot of seminars outside of the Research and Early Development Group. We have a program we call gRED, the Genentech Research and Early Development Revealed, where we go on and give talks around the whole company, to the finance group, to the sales folks about the kind of things that we're doing. So pretty standard things, Web-based applications and seminars and so on. A lot of the data actually eventually comes out in press releases and people see...

We post and everybody gets an email everyday with the press releases that have come out. And we have to announce material things to the investment community in a very regulated way so that everybody finds out at the same time. So that certain people don't find out ahead of time and manipulate the stock and so on. So people get an email everyday with the press releases. Sometimes, things are kept somewhat confidential until then. Just because once you tell your few thousand best friends, somebody's going to be at a cocktail party with a broker and have three martinis and can actually get in trouble for that kind of thing, if you're not careful. OK. Question back there? Yes, thank you. My question, you mentioned you're kind of introverted nature when you're in research in academia, which I would think is generalize-able. And now, you manage all those fleet of people who focus on research.

So my question is, I'd love to hear about how you motivate such a workforce that might not be as extensively motivated and

how do you incentivize them? So... The question. The question is how I'm sort of inward-looking and coming from academia and so on, worked in the lab, sort of been with my students and so on. But now, I have a thousand people that work for me, how do someone like me motivate folks? So, at Genentech, we work a lot on our culture. We spend a lot of time thinking about our culture. I have a leadership team. We motivate people by the fact that we are doing work that we believe will really, really help patients and sick people. And if you think about, if I think about, the kinds of molecules that we have in clinical development for things like Alzheimer's disease, asthma, cancer, infectious disease, psychiatric disorders, if our portfolio plays out reasonably successfully over the next decade, it could actually be the case that we will rather directly affect every family in the developed world. I mean, who doesn't know someone in their family that had one of those diseases? So, we really, really help patients and that is extremely motivating to me. And to unblind, the clinical trial, especially on oncology clinical trial where you give half the patients the drug and half the patients a placebo.

And the end point is how fast they die. I mean, to unblind the clinical trial like that and to see that you've made a difference is really, really... Most, I mean the room usually starts crying. It's really really... So the first thing is, meaningful work. We believe we do meaningful work and we talk about it. So I had a town hall last week so all 2,000 people. We had a patient come and talk. The patient is taking a hedgehog inhibitor. It's for a number of diseases but largely basal cell carcinoma.

This guy had a disease called Gorlin's Disease. It's fairly rare but it's a basal cell disease again where you get large growth and if they're not surgically removed, they can be... Mostly they start on your face and then your trunk. He's had it his whole life, it can be fist size. And he's a salesman. And he said, "My whole life I went out doing sales and I had big scars all over." A chunk of his ear is gone. This is a targeted drug. It's a mutation in the pathway that gives rise to this disease. He takes our drug, all the lesions are gone. He doesn't had one since he started taking the drug.

He was so thankful. I think that's a big, big motivator for our industry and it's maybe a little different than other industries. I mean, I'm sure I love iPhones but they don't save my-probably does save my life actually. I couldn't say that. But it's a little different. So I think that's really the number one thing. And then we motivate people through, there's always compensation. So we have three components to our compensation: salary, stock and bonus. We target salaries at the 50th percentile of the market and we have a target bonus that's at the 50th percentile. But there's tremendous upside depending on the performance of the company and the performance of the individual.

Did you move a molecule into the clinic? Did you publish a bunch of great papers? Were you the lead clinical scientist on a Phase II study where the design was terrific and it worked, et cetera, et cetera. So, bonus, and of course, stock which tracks with the overall performance of the company. So, I think those would be-I can talk about that for a long time-but I think those would be the two major things. Great. You mentioned basically two big differences between industry and academia as being a first specificity, that as a professor you tell your students what to do and they come back some indeterminate time later, they may or may not have done it. And also, feed back, which in academia either going up or down is often either vague or lacking. Do you have any thoughts on how industry practices and cultures might potentially benefit academia in some ways? Yeah, I think that it would have been better for me if I brought in some of the HR, if you will, practices from industry into academia and provided more direct feedback, to provide better career counseling. I don't think though that the way projects are managed would work, as in industry, would work in academia. I don't think it would have helped to have timelines and things. It's just sort of more rigor behind the organization of the projects.

I think the kind of spontaneous creativity that comes in industry without people's discretionary time in an academia with the way projects are done, I think it's best to be a little less organized and to have some churn to it. I wish that I could even get sort of more churn into Genentech and a little less reverent kind of behavior. I think that would help with our ability to innovate. Career counseling, I think it's done more now at Stanford than it was 10 years ago when I left. I spoke about three weeks ago over in the medical school. I think career counseling is an important thing that's done. It's done much better now in academia, this kind of forum, than it was ten years ago. We also talk about how we inspire people. We have a goal this year that of our 2,000 people, 90 percent or more of the people have what we call a development plan. Our manager sits down with a person, "What do you want to do with your life?" "Where would you like to be in ten years?' "OK, let's think about how we can get you there." "Maybe, it would help if you would sit in this team." Or, "Maybe it would help if you took this course." Whatever.

So everybody has a development plan. Not that they're all get to where they want to be but so that they very clearly define with their manager a plan to advance. Or people just say, "I love what I'm doing. I just don't want to be bothered. Just leave me alone. I don't want a development plan." That counts in the 90 percent we tried. So I think that kind of thing, brought back a little more formally into academia would be good. Great. Go ahead. Being in the pharmaceutical industry, I guess you've faced a lot of ethical issues.

Say a drug can help a lot of people but perhaps is not profitable. How do you, as a manager and as a leader, manage those issues. There are ethical issues everyday. There are a lot of ethical issues around the clinical trials. For example, you have a drug that you're pretty sure is going to work and we're required in a number of cases by the FDA to have a placebo group. And nobody wants to be in the placebo when we're doing a survival trial. Nobody wants to be in the placebo group, and

one could question whether it's ethical to even have a placebo group or whether you should just put everyone on the drug and compare it to historical standards, which of course is not as good an experiment, that's for sure. But these are real folks that you're treating. So a lot of our issues around our clinical trials are basically determined by the FDA, where they tell us, "No placebo control, no approval, no drug for anybody." So we're required in a lot of cases and we often-often-we sometimes disagree with the FDA on whether it's ethical to have a placebo group. But in the end, they're the regulators and they would rather be really, really sure that you have a drug that makes a difference that you can then market to hundreds of thousands or million people than to...

And maybe for some folks, not to get the drug early on and to be sure in the end that it's a good drug. So a lot of our ethical issues around our clinical trials are determined by the regulatory agencies and we basically just have to follow what they say. Now, in terms of drugs and their use in the third world, we wouldn't, frankly, try and make a drug for a third world country disease because it's not profitable. And fortunately, there are groups like the Gates Foundation now that are putting that kind of money into those kinds of clinical development work, that are starting to think more about that. But we can't justify to the people that buy our stock everyday that we are going to spend $1.5 billion and then give it away. Now that's for better or for worse, and that's not the way the western world functions nowadays. If it's free enterprise, it's going to determine what drugs are made. And it's a growth hopefully driven business, I have to justify at the end that there's some return on the investment that I make. In the United States, for example though, it was really a bit of a fallacy that our health care system was so terrible. I mean, in terms of prescription drugs, if you have insurance, insurance pays.

If you have insurance and you have to make a co-payment and sometimes on an expensive drug, the co-payment can be more money than someone will have. So if you couldn't afford the co-payment, we paid it. And if you didn't have any insurance and you needed the drug, we just gave people the drug. So somebody wanted to do a... 60 Minutes wanted to do a story once on one of our expensive cancer drugs and to find somebody that was dying because they couldn't get the drug and make us look bad. But you know what, they couldn't find anyone who wasn't getting the drug. So that drug, we've given away, I don't remember what the number is, billion dollars worth of free drug. We spend a lot of money every year on co-payments for folks. So we believe that, least in the Western world where we operate, everybody has access to our drugs, even if we just give it to them for free. OK.

Let me take one more question. OK, great. Speak up, more though. You said that you were hired because you're a very good scientist? How much science are you using in your job versus the management and leadership skills? And do you miss anything really actually being a part of core science and do you think you'll ever go back there? Well, that's a good question. Well, so what did I do today? So at 9:30, I had a phone call with two scientists at the Cold Spring Harbor Lab in New York, who have an idea that they think would be useful in breast cancer. From 10:00, for four hours, I went and heard a bunch of research presentations on a strategy in angiogenesis and so on. And so a lot of what I do, as I said, is hearing about the science and the clinical trials. I have a model where there's a single decision, accountable decision maker. This is quite important for every decision that is made. So that in this Research Review Committee meeting today, there were alternating chairs depending on the topic and the chair is the decision-maker.

The chair reports to me but I don't decide unless I think that the decision is really, really kooky and very, very expensive. I could overrule someone but that rarely happens. So in terms of the decisions that are made throughout the group, I generally don't make them. But I need to feel though I understand them and agree them so I'm in many of these scientific meetings hearing about the programs that were going on and sort of course-correcting this big ship maybe by a degree or two here and there when I need to. And I think that most of the leadership problems that I run into, it's more... You can go really far in life with a little common sense. The kinds of leadership issues that come up, I just sort of resort back to my roots and my beliefs and why I'm at Genentech. If you keep patients in mind, and if you're always doing the best thing for patients in your decisions, usually, it's just pretty clear what to do. So it's sort of hard for me to say much more than that. And by the way, I have a small lab.

So I have every Tuesday at noon, a lab meeting. And most of the higher level management people at Genentech have a lab. I think that's really, really important. Otherwise, it gets too easy. You go sit and some big room and someone makes a presentation, you say, "Do this, spend some money here, do that," You forget how hard it is to actually make an experiment work unless you're sitting with your lab group. And you see oh "Jeez, it didn't work again. What are we going to do?" It keeps you grounded in reality. So I think that's extremely important and I'm extremely proud of the fact that the high level scientist at Genentech still have labs and write papers and so on. Would I want to come back? Well, I don't know. Probably not, and the reason is, I think the university works unbelievably well, given that it's just completely unclear who's in charge.

And I don't think I could stand that anymore. I need to know. Well, you know, I think you'll call back in the end. I need to know who's in charge. I'm going to be in charge. And who'll be deciding. I'm going to be in charge right now. And I'm going to ask everyone to join me in a huge round of applause.