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Relentless Pursuit of Innovation [Entire Talk]

Susan Desmond-Hellmann, *UCSF*

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UCSF Chancellor Susan Desmond-Hellmann has a track record of fostering environments conducive to innovation, in both the public and private sector. In this engaging lecture, the renowned oncologist shares insights from her career in biotechnology and academia on leading teams, managing risks against rewards, and innovative product development. Desmond-Hellmann also shares her belief as to why entrepreneurs must remain relentless when it comes to pursuing their goals.

Transcript

I have the pleasure in introducing Susan. She is the Chancellor of UCSF. And that's essentially the same as our own President John Hennessy here at Stanford. UCSF is special to me. I'm a Berkeley graduate, and that's one of the other campuses, but UCSF is one of the ten campuses of the University of California. It's a medical school doing incredible research in that area, teaching graduate students in that area, and like our own hospital here, providing patient care. Sue was at this company I'm sure you've heard about, Genentech, for many, many years. I mean, she started her career years before that but she was at Genentech for many, many years and including the President of Product Development. We tried to have her here in the series during that period. So we kept at it and we were successful today.

I don't know if you got to see the bio but this is pretty remarkable. At least over a year ago, Forbes Magazine named Chancellor Desmond-Hellmann as one of the world's seven most powerful innovators, calling her "a hero to the legions of cancer patients." How many of you had a family member that was touched by that? My mother, yeah. And I'm sure others share that. So this makes it an incredible day. The all seven of them were lauded for their curiosity, empathy and leadership. Those are all parts of why we do this seminar series. So when it came up that we had the chance to have Sue come and join us, it was an absolute no-brainer. So let's give Susan Desmond-Hellman a big Stanford welcome. Thank you for that kind introduction and welcome everyone. I am so happy to be here.

It's a beautiful day, the campus looks great. We have at UCSF what's called an urban campus. Many fewer palm trees than you have here. So I have an agenda. I don't have slides because I thought that maybe I would just tell a few stories. I like to tell stories and I wanted to introduce you to being an entrepreneur and a leader in life sciences by introducing you a little bit to my journey and talking about some of the differences in how you can innovate or attack problems in life sciences from many different angles. So as you've just heard, I made a very unusual move from Genentech back to University of California, San Francisco. But before that, after I was a student like you all are now, I had a very unusual and atypical journey. And I want to start by telling you a little bit about that, because I think it frames how I think about leadership and how I think about innovation. After I went to medical school, I came to UCSF to be a resident, which made you do your clinical training in internal medicine.

So that's the path where you're a general medical doctor. After four years of doing that, and learning medicine on the wards in San Francisco, I decided to do an oncology fellowship. So I wanted to specialize in cancer. I wanted to be an adult cancer physician. And while I was in my first year, I got very, very interested in why people get cancer and decided that I wanted to be a cancer epidemiologist, to study the natural history of cancer to specifically impact on patients not getting cancer. I think I was ahead of my time because everyone now thinks about health, wellness, and disease prevention. But we didn't have a lot of

tools then, other than "Stop Smoking" which is the best way to avoid cancer and remains the best way to avoid cancer. But because of that interest I had, when I was a second year oncology fellow, when many of my colleagues went into the lab and started working on basic research, I did something very different. I went across the bay to UC, Berkeley and got a masters degree in Public Health, with a specific focus on epidemiology and biostatistics because I wanted to learn more about methodology to become a cancer epidemiologist. I wanted to learn about things like P-values and inference and proving things like one does when you're trying to prove, for example, that something causes cancer-or does not cause cancer.

And that was a life changing experience for me. It gave me a fantastic fundamental background for the way I think today and the way that I use that inference-proof, those concepts, later in my career. Now, as all of you know, you can have a very good notion of what you'll do in your career and then life intervenes. So what made a big intervention on my path as a clinician when I was in UCSF was the HIV/AIDS epidemic. Over the years, as I studied medicine and cancer, I became an expert in the kind of cancer that was most prevalent associated with the AIDS epidemic, Kaposi's sarcoma, and got into the study of Kaposi's sarcoma. Again, the ideology, why did patients who had HIV infection developed Kaposi's sarcoma? And as I was asking questions about that, two things happened. One, the Rockefeller Foundation approached UCSF and asked UCSF to start to study AIDS in Africa; and secondly, I decided as I was investigating Kaposi's sarcoma to try and understand African Kaposi's sarcoma which had existed for a long time before the AIDS epidemic. So before it was popular for students to go into international health or global health, my husband, who's an infectious disease doctor, and I were loaned by UCSF to Makerere University in Kampala, Uganda. And I became the attending physician at Uganda Cancer Institute studying epidemic or HIV-associated Kaposi's sarcoma and endemic Kaposi's sarcoma, the kind of Kaposi's sarcoma had long been seen in Africa. A fantastic experience in global health.

Following that experience, I went into private practice. I was what my parents now called "a real doctor". They might seem slightly disappointed when they say that. I put on my shingle and every day, all day long, I saw patients with cancer. That was an experience that was one of the most amazing things that I had experienced in my career. For two reasons, one is, being a real doctor every single day lead me to understand cancer in a very different level than I had before, as someone who approach it from much more of a research standpoint. I learned much more about caring, healing, side effects and compassion as they were associated with patients with cancer. And the other thing I learned is, cancer is a lousy business. And when I was in practice, we had too few remedies for what I cared about most which was healing patients. Making them all better, helping.

And so, after a couple of years in practice, I made another career change and went to Bristol-Myers Squibb, which was the first experience I had in cancer product development. So Bristol-Myers Squibb is and was then a very traditional pharma company. What's called Big Pharma, a very traditional, typically a chemistry type of company that uses chemistry to make small molecules and have a long tradition of cancer therapy. And at the time, I went there Bristol-Myers Squibb had a new drug called Taxol, paclitaxel, which was a new cancer drug that was specifically being designed for breast cancer at that time. So I worked on Taxol for breast cancer for two years. Very traditional. Very traditional. And it went very well. We were able to have Taxol approved for the treatment of breast cancer in the US and Europe where it remains a mainstay of breast cancer therapy after many years have passed. I tell you this background because I think one of the things that impacted me as an entrepreneur and as a leader was that journey.

So I was so privileged to be able to learn epi and biostats, some of the fundamental principles of how one thinks about product development, how to be a doctor, how to care for patients, and think about what's good for patients, and very traditional pharmaceutical approach to product development. So today, I am at University of California, San Francisco-as you just heard, one of the ten UC campuses-after a 14-year career at Genentech in biotechnology. And what I thought I might do to help you understand and frame a little bit of how I think of entrepreneurship and innovation in the private sector or biotech and at UCSF, in the academic sector, is just tell you two stories. I remained passionate about product development and innovation as it relates to helping patients and I've had the privilege of doing so in very different settings. I want to tell you two stories that I think help you understand a little bit more about how one thinks about innovation in biotech and innovation in academia. Let me tell the story first about developing Herceptin at Genentech. So I left Bristol-Myers Squibb in 1995 and came to Genentech, which was the first biotech company and founded in 1976 based on recombinant DNA technology. Which was co-discovered at UCSF and Stanford. So that discovery of recombinant DNA technology started an industry. And I was thrilled when I got to Genentech to find out that it could be possible to treat cancer patients potentially without the side effects of nausea, vomiting, hair loss and bone marrow suppression, trying to use biology to treat cancer instead of chemistry to treat cancer like Taxol.

So, the development of Herceptin was an extremely innovative project. And let me tell you three ways in which Herceptin was fundamentally different than anything I had ever been able to bring to cancer patients. First and foremost, Herceptin was the first time ever that a monoclonal antibody, a human-like monoclonal antibody-like we all make in our immune system-could be brought in large amounts to patients with a solid tumor. A very, very scary disease, fast growing and likely to kill the patient. Now, at the time monoclonal antibodies, being natural, being humanlike, were thought to be gentler treatments. And in fact people use to have a slogan, "Could you have a kinder, gentler treatment for cancer?" And I was a little puzzled by that. Having seen so many cancer patients, I didn't want to be kind and gentle when it came to the therapy of cancer. I wanted to wallop that

cancer without causing side effects. But this monoclonal antibody therapy, for the most difficult to treat breast cancer, was completely innovative. And we were relatively pessimistic about it.

One of the things I learned from that experience is don't be afraid to take risk and try something, even if everyone's skeptical. And every one was. The second thing that was innovative about Herceptin and now it seems routine, but at that time, it was incredibly innovative. Could you treat only the breast cancers that were driven by an oncogene, a growth factor for that cancer called HER2. Only one in five of the patients with breast cancer had that driver. Therefore, we would only treat that one patient out of five whose cancer was dependent on HER2 to drive its growth. Personalized medicine, targeted therapy-now popular, while not routine, definitely the best way to treat patients but incredible novel. What that meant for the regulatory path is we had to go to FDA and ask for approval for the therapeutic and the diagnostic at the same time. Extremely hard, and very novel. And the third thing that was so special about this is that the engineers, in manufacturing, had to be ready with the biotech process for making this antibody reliably using Chinese hamster ovary cells at the same time we were ready with the therapeutic.

So you had to work in teams effectively, with a large team that could go to FDA. The experience of working in biotechnology to make the first antibody that had been approved for use in breast cancer was an amazing experience for me. And in the end taught me not just all those technical things, which we were able to overcome and obtained approval in 1998, but much more importantly, not to underestimate what was possible. I always thought that you had to be in discovery, that you had to have that sort of test tube in one hand and light bulb going off over your head in the other hand to do something innovative. And as a clinician, I didn't see myself as an innovator. But that opportunity to take what have been made in the labs and bring it into clinical trials, use all those things I had learned about inference and proof in showing that Herceptin was good for patients with HER2-driven breast cancer, I could be an innovator. A big breakthrough for me, personally, and something that my group, who were the "D" of R&Dat Genentech, could take great pride in. So a very focused product-driven innovation to bring something through the Food and Drug Administration, to patients and other regulatory agencies, to bring this product to market worldwide. Now, reel forward 14 years, that was one of the great innovation experiences I had at Genentech. So in the summer of 2009, I left Genentech and returned to UCSF as Chancellor.

And students often ask me, "What does a Chancellor do anyway?" Which I find both endearing and a little daunting. And so, what the Chancellor does is the Chancellor makes sure that the University, the citizens of UCSF, have the resources and talent they need to execute our mission. So I like the description of UCSF, that we're one of ten campuses and we're the life science campus. I describe UCSF sometimes by what we don't have. No football team or basketball, no English majors and no undergrads. UCSF is only a life sciences graduate school, with the School of Medicine, Dentistry, Pharmacy, Nursing and a Graduate division. Tiny, students-3,000 professional students, about 4,500 trainees total at UCSF. Very specialized. So as Chancellor, what do I do, for example, for patients with breast cancer now that I've left my job in product development? Well, I wanted to tell you a story about innovation in breast cancer that's going on at UCSF to just describe what I think is possible in academia, that's tremendously exciting to me. And as Chancellor, I want to create the kind of environment that allows for that kind of innovation.

So there's a trial that's going on at UCSF called the I-SPY2 trial. The name's not as important as what the trial's trying to do. Today, if you tried to make a new Herceptin, on average, it will take you 12 years and a billion dollars. I don't like that. Those numbers are lousy. So that if five people in this room got ideas about new breast cancer drugs, we need to raise a capital for those five ideas and take that kind of time? And at some level, I think I want things to improve in our lifetimes, for our generation as baby boomers, the generation after us, our parents. So what can I do? What can we do in academia to enhance our ability to innovate more quickly, to improve cycle time? Well, what I-SPY2 does is it's a trial of multiple therapies rapidly tested in sequence. And those therapies are tested at a particular moment in time before a woman with breast cancer has her primary surgery. So the really brilliant thing about this trial is that you can use a pick-the-winner strategy. You can cycle through multiple therapies and you pick the winner on two basis.

One is, when you do the surgery, is any of the breast cancer left? So you get a rapid readout. You could actually check the surgical specimen and see if any of the breast cancer's left. And secondly, toxicity, so you can throw out a product if it's ineffective or unsafe. And, the trial combines imaging and biomarkers so that we can iterate and learn one product after another. We can also put combinations of therapies into this fast readout method of testing breast cancer drugs. That wouldn't be possible at one company. Unless you have a huge stable of breast cancer drugs which is not, today, the case at any company. We're working with more than five companies to bring many products into this system and iterate and test them rapidly. And having that kind of environment, where our contracts and grants office, our intellectual property, can allow for us to collaborate effectively and innovate on the technical aspects of breast cancer studies. So that as new discoveries are made, we can make things go faster and more efficient.

Because asking and answering questions efficiently in life sciences is something we don't do yet, and I think we need to do. So the I-SPY2 trial for me is a wonderful way in academia for us to have a system in collaboration with innovators in the private

industry or in government that can allow for things to go to product development quickly. So a couple of lessons that I've learned in leadership and in innovation, both at Genentech and at UCSF, I wanted to share with you in this class. First of all, one of the things that I think is most challenging about anything that needs to be orderly. And I know many of you are engineers. Some of you are in health sciences or life sciences. There's something very important about being a life sciences innovator. And that is that we don't have an experimental system. We have a human being. So the human beings who were involved in the trials, their protection, their wellbeing, has to come first and foremost before anything.

So think of yourself as wanting to hire, recruit, retain, reward innovators, risk-takers, in a world that involves human beings. So what I learned more than anything is to be really clear on when it's time to take risk, when it's time to say, "Gee whiz, I wonder if we could try that," and when it's time to be very orderly. An example, when you're doing something that requires sterility. Sterility is an essential part of taking care of patients. When you put something in someone's vein systemically, it has to be sterile or they get a Bacteraemia. Very bad outcomes. There's not a lot of wiggle room on sterility, right? There are things involved in manufacturing, things involved in running a hospital which we do at UCSF, that involve compliant behavior, regulatory behavior, doing things the same way all the time-the six sigma kind of operating style. One of the great challenges, a very important challenge, is having room at UCSF for people who show up at noon and work all night, when right down the hall is somebody who shows up and punches a time clock and works on sterility. And a great leader has to have an operating style that works for both of those people. And is really clear about what behaviors we want, reward and risk-taking when risk-taking can pay off and not have bad side effects.

I think that's extremely important. The other thing that I took from private industry and brought to UCSF is the whole question of, "How do you incent the kind of behavior you want?" So, principal investigators tend to be rewarded for solo behavior. Are you first author or last author on a paper? Are you going to win a prize-the Nobel Prize? Are you going to publish? Are you going to get you a grant? Many of the things we need to accomplish in science and medicine today are team-driven. What if you made a huge contribution to the team and you didn't get on the paper or you were third author over and over? Can you progress? Can you get promoted? Can you win prizes and be recognized? A huge issue across all team-based science and something that I'm passionate about, rewarding team behavior. So pushing to team prizes and making sure that collaboration is rewarded in a system that has for a long time rewarded individual behavior. Something that as Chancellor, I can promote and celebrate that kind of team behavior that's good for patients and good for the kinds of outcomes that we want. I want to leave most of time for questions but I wanted to my end my prepared remarks with two big ideas. And I know this building and this campus is filled with big ideas. If you're reading the papers, you would read this week that the Food and Drug Administration here in the US has just rejected their third in a row new obesity drug. Remember what I said about the 12 years and the one billion? Picture yourself being at a finish line for approval after, let's say, 700 million to $1.2 billion and years and years of basic research and clinical trials with a new obesity drug.

The most recent one, you can read about it in the paper. You go and you say to the Food and Drug Administration, "The patient lost on average 4 1/2 pounds." That's actually the truth, I didn't make that up. And FDA says, "Well, see, we wonder in ten years, if more patients were treated with this might get heart disease than the patients who didn't get this. So we want you to do that study, Company A. And come back in ten years and tell us if that 4 1/2 pounds of average weight loss was accompanied by an excess of cardiovascular, more heart attacks and strokes. Because if that's the case, that's bad for you." So the net of these three bad outcomes in a row, inevitably, will be companies who are smart, and companies tend to be smart, aren't going to develop new obesity drugs. Because they see this very long journey that's expensive and questions that come up about long term safety. So one of the big ideas I have, and I know you've had speakers who have talked about regulation particularly in the device side of the industry. One of the biggest challenges in my opinion on making new innovative products in life sciences is the binary outcome of FDA approval. So put yourself in the shoes of an FDA Reviewer.

So you're in charge of reviewing the new drug and you have two outcomes. Yes, this is safe and effective for obesity, and perhaps millions of patients are going to be exposed to that drug and if they do have an excess of heart attacks, it's your fault. How often are you going to say no? Always. There's no benefit to you to say yes, and all the risk is on you, because you've only got an answer of yes or no. Well, if you really follow product approvals and the course of product approvals and all of what's been in the paper about side effects, you'll know that life doesn't come in binary. It's a maybe. So maybe this drug is safe and effective after ten years and maybe not. The reality is we don't know at the time of product approval what the long-term consequences of new medicines are. So my big idea is to give FDA and that poor reviewer, all of the onus on them to protect patients from side effects but also wanting to give therapeutic benefit, to treat it as a continuous variable rather than a dichotomous variable. A continuous variable would have a range of certainty, of confidence.

And that confidence would come over time. So for example, the FDA could say no. "Four and a half pounds, that's not enough. That's not enough any side effects acceptable." On the other hand, let's say, it was ten pounds but you still have uncertainty. You could have an approval process that started out with a low level approval. You don't get a sales force, you can't promote that drug and you can't put TV ads on it. But you could sell it. Then you increase your confidence. "We haven't seen any heart attacks after five years, Looking good. The ten pounds is really holding up and in fact, some of the patients as

they stay on the drug longer, lost 15 pounds.

OK, maybe you can have a sales force. Still no ads on TV." Then you gain more confidence, it gets to be eight years. Is there a system where we could, as we increase our confidence in safety and advocacy, allow for broader distribution and more promotion. Not a yes or a no answer. I think that could really change two things. One is, the odds in the business model would be more stacked in favor of investing in difficult things like obesity, type 2 diabetes, high blood pressure that were at risk for no innovations. And the other thing is we could improve how we communicate to the public. Instead of saying, "Yeah, I saw that on TV. It must be perfect. You can't have side effects and put it on the nightly news." We're doing a lousy job of communicating to patients that all medicines have consequences.

So, if instead of saying "We're 100% sure it's good for you and not bad for you" to communicate "Every medicine has a consequence. Every medicine has a side effect and this one we have a lot of confidence or poor confidence." So I think that would completely change things. The other big idea that we've implemented at UCSF and is in its very early stages is the degree granting program called an MTM, a Masters of Translational Medicine. And this is a program designed to bring together life sciences experts, physicians, and scientists with engineers, computational experts, bio-informatics experts to see if there are ways of bringing these two discipline areas together, that we can increase the likelihood of success. Increase the reliability and predictability of what we do in medicine. And ultimately, what I would love to see is could we innovate in life sciences to bring down costs. So as I watch the high-tech industry and I'm a consumer of high-tech products. Every time I buy a new iPod, it's better and cheaper. Every time someone comes to my hospital for a new X-ray, it's better. It's not cheaper.

So what would it look like in life sciences that as we iterate each subsequent generation of product it's less expensive and more reliable. And if we don't accept that challenge, we'll price ourselves out of business in the health sciences area and maybe already are. But what would it take to innovate in product development, in delivery, and in how we think about health and wellness that could really change the game? And I think by putting the brightest minds together, it gives me some confidence so that's where we'll end up in by the future. So, I'm going to stop there and happy to answer questions about any of that or anything else you'd like to ask me. Thank you for listening. That was terrific. I'm going to take a page from Tina's book the last couple of weeks and help moderate their questions. I especially encourage Professor Roysen's class, the MS&E178 students who meet afterwards, to kick us off. Anyone like to do that? Anyone else like to do that? All right, well, I'll kick it off first. All right, thank you.

You guys, after me. We have lots of questions on Monday. Thank you, though. That's really, really interesting and one of the things we talked a lot about is we study entrepreneurship. So we talked about your life before becoming Chancellor and all the entrepreneurial things that you did and we were curious about your decision to go to academia. What kind of challenges, what kind of differences do you face in recruiting, retaining, motivating people in the academic world versus what you had in Genentech and how you're dealing with them? Maybe the biggest surprises and the things you're trying to accomplish in that route? So, I would say that the...And I'll start with me. So I made the decision to move from Genentech to UCSF in part because Genentech became a wholly-owned subsidiary of Roche and so my group became a global division of Roche. And so for me, as a leader, I really loved the fact that we ran the company. I just thought that was so inspiring and so amazing to be able to set the values, the direction of a company and I couldn't imagine not doing that anymore. I just really loved that part of my life at Genentech and I was inspired to take on a leadership role at UCSF for that same reason.

I think it is both daunting and inspiring to think of a larger organization. UCSF has 23,000 people and thinking about all those people collectively and what can I do as chancellor to help them succeed is really inspiring to me. So that was the main motivator for me to make the shift. I also was very inspired to get back closer to teaching and to patient care, both of which I missed greatly in going to industry. When I was at Genentech, there were two things that I loved about leading at Genentech. One was that we had such a clear and simple purpose. We wanted to use the science of that biotechnology to improve outcome from patients. And in my group, we wanted to take those basic discoveries from the lab, test them in clinical trials, and then get them approved for sale. That was the group's job. And when I first got to Genentech, many people thought that that meant that it was fate whether we succeeded or not.

It's biology, it's medicine, and that it was not in our control whether drugs were safe and effective. We just tested them and there was a somewhat passive nature to that and I didn't think any much should pay us if it was fate. We're supposed to make good outcomes occur. Not every time, but the outcome should have been that we advance the mission by getting products approved. What we did at Genentech and I think it helped us meet our goals is we broke down every year into a set of corporate goals that were measurable. So we put in place metrics and accountability and we put a bonus program in place for the whole company that were around those metrics. So, enroll a certain number patients in the clinical trials, obtain FDA approval, get a label that included something in the label that was important for us. And I was so amazed to find out, one, that it was perfectly achievable in R&Dto set metrics that were achievable and measurable; and two, that in fact people do what you reward them for. So, you can set a common tone with corporate goals. They're measurable.

They're reward-able and the entire company would point in the same direction. Then, when we got Herceptin approved in

1998, before we were finished with manufacturing additional Herceptin, patients had to go to a lottery to get this life-saving drug. We literally had half the company down packaging the Herceptin vials because we were so motivated to get it out for patients. You don't need a bonus to do that. You know patients are waiting. But for the things that are... The steps along the way, where you can't see a patient directly benefit, breaking it down into metrics and rewarding that. At UCSF, one of the things that I think-and this is true with any university-that I found really challenging when I first came was to try and to find what we all had in common. When I would meet people and they would say, "Well, I'm a pediatrician at San Francisco General and I'm really caring for the uninsured and I'm passionate about that. And I show up every day for work happy to teach students and care for these kids." And then, I would meet someone else who was doing a basic biology of how the mitochondria works in the face of lupus and I would try and think, "Okay, what is it that the pediatrician at San Francisco General and the basic scientist at Mission Bay share in common?" And our tag line at UCSF is advancing health worldwide and that is very inspirational.

It's what we all have in common as a health sciences campus and I thought that was great. That was really clear that that what's we have in common is our persona, our mission, our values. What about rewards? So how do you put in place our reward system for those individuals who have such a big diversity of what they work on and their outcomes, and including teaching outcomes. How do our students do? What our graduation rates? I think that has to be done locally. When you're in academia and you much more care about the institution's brand-what does UCSF stands for, the mission, the values and the environment that allows people to have their resources-but locally they had to set the goals and the rewards system. And I found that to be... The fact that I had in hand those corporate goals and that reward system that was so simple in retrospect, it's much more complicated in academia. And I think that people are much more motivated by two things. One is, individual success in academia is more rewarded, more commonly, than team success. And they're much more rewarded and inspired by the public good which does drive people to work for a university and in the public sector.

And I think you can take advantage of both of those to drive outcome. May I just do a little follow-up to that, in somewhat of follow-up. So, I know some of your faculty at UCSF and they share our desire as part of a mission to teach entrepreneurship and teach innovation, and especially how may you deal with skill development. So in your mind, what are those skills? I mean, is it covered with change? Is it being a good team mate? Or what do you think are the key skills that we should be teaching here and to these students and what your faculty should be slipping into their courses at UCSF? So, the people who I've seen succeed as entrepreneurs... There are two things I would point out, that I observed and that are true, over and over again. There are many things that are corky. Or an individual succeed, I think, when as probably not reproducible, that maybe a 'one offer good luck' because luck is actually really helpful whenever you can get it. Be lucky. But the two thing that are very much important, one is this doggedness -- impatience, relentlessness. We used to have a saying that I like, like "someone's like a dog on a bone".

Many of entrepreneurs who are successful who I know are like a 'dog on a bone'. They just won't leave it alone. I have been teased about when people would see me... When I worked in South San Francisco, I eventually only took public transportation, and you'll know why in a minute. I would be at a stop sign or a stop light and the stop light would change colors several times and I would be sitting there with my head down muttering. And the reason, I was just thinking, "What can we do?" Like, "We got to enroll that trial faster. We got to get that answer. We got to...". And I was just... I couldn't turn it off and I just could not stop thinking and just...

In that sense of relentlessness, of staying awake all night, staying up all night and you just can't let it go. Solving a problem, you don't accept that it's unsolvable. And I think part of that is believing that if you work hard, surround yourself with smart people, keep thinking, keep trying that you will solve that problem. It's also relentlessness with optimism, I think, and they tend to travel together. And the other one is being unafraid to be embarrassed. I remember telling somebody that we were going to make a huge difference in cancer patients with this new way of treating cancer patients with antibodies. I still remember the conversation, the guy I was talking to literally, in front of me, rolled his eyes, like you guys. It's going to be so embarrassing when you've spent your company's money and you've done this and you, Sue, move from the number one cancer company in America, Bristol-Myers Squibb, traditional, great cancer company to Genentech? What are you thinking? Do you have a backup strategy? It's going to look bad that you moved from this great job you had. And I thought not at all about whether it would look bad. And I would say the same about coming to UCSF.

You asked why I would go to UCSF. In my litany of what could go wrong, none of that was "I would be embarrassed." And people who are risk-takers, who are entrepreneurs, who are willing to change careers, try something different, don't think of what others think of you. Think about the purpose or the outcomes you want. I think those two things, being dogged and relentless to the point where some of the entrepreneurs had worked around aren't really that much fun. You don't want to be with them at a party, but boy, you want to be on their team if you're on a new venture. So now that you said that, follow-up question, and I know you won't mind my asking this. Because you just said you're not afraid to be embarrassed by me. Now, you guys are doing your best to embarrass me. Great. Can we talked about though is that the role you're really taking on is that of somewhat of a public figure.

And you had to deal with things - personal shareholdings, labor, things like that. How do you deal with that and what would you recommend to the students who ultimately face those sorts of challenges. And how much of your time do you spend dealing with those sorts of things? What's your strategy for that? Well, that is the part of my job that I probably underestimated, which is that, when you take on a role like this particularly at a public university, you're like the mayor in many ways. There's a lot of rules that govern what I do and don't do. There's the Public Records Act, that anybody who wants can ask for my emails and my trip reports and things like that, and my stockholdings, and gift, and travel and so forth. How do I deal with that? Well, what I try to do is two things. One is, I've always had a wish to make sure that having worked in a highly regulated industry and with patience for so much of my life, my most important compass is inside. Not the newspaper, not what people say about me and it is very possible for me to disappoint myself and nobody knew it. I like that saying "I'm my own harshest critic." I am so my own harshest critic. So, one is, to make sure that in being a public figure, I don't turn towards avoiding what the paper says about me or the union say about me or whatever as my metric and keep my internal compass of what I expect from myself, but also to understand that in this role, I represent the university.

So the stakes are different. It isn't me, Sue Hellman, private citizen. It's me as representing the university and what we stand for and what we do. So it takes a lot of self-coaching. Right there. How close dependent or independent do you think academic institutions like UCSF should be from industry or the industry they work in? I think that there's something really... Yeah, this is a question about the independence of organizations like UCSF from industry. So the perception or the reality of conflicts of interest and directions from industry to public institutions or universities, and I think it's an essential question. It gets to something that I value very much about being UCSF and being in university and that is trust. There are two things that we have to balance when we interact with anybody -- with a patient, with an institution, with the government, with private industry -- but particularly with private industry.

And those two things that we have to balance are the trust and confidence that the public places in us and our faculty to say truth. Not truth as per somebody who's giving their money but truth as they understand it today, to the best of their ability, and that is a very precious thing. It's hard to gain and it's easy to lose. So that has to be balanced with a fact. And the fact is, UCSF does not commercialize products. So, if someone at UCSF makes a discovery, be it a device, a new operation, a new medicine and wants to commercialize that, that will be done by private industry. For me, the need to keep that trust and confidence means that we have to set up contracts and procedures and transparency, that enables that industry interaction and collaboration without impacting in a negative way the public's trust and confidence. But what I don't want us to do is scare people away from working with industry, which I think is not only acceptable but can be a real positive. So I don't want people to get a scarlet letter and I don't want to drive people into secrecy. I want it to be transparent and easy for them to work with industry.

Where it gets really hard is in the procedure area. So, it works very easy as when you're working on experimental system that don't involved humans. As you get into humans, that's much harder and as you get into procedures, it's extremely hard and here is why. So let's say I made a new catheter and that catheter is really good for patients who just had a heart attack to avoid the next heart attack. And I'm really good at putting that catheter in, best in the world. And you come to me and there's five other catheters but I'm really sure that mine is the best and I'm the best at putting it in. So who should give you advice about your catheter and who should put it in? Me? I'm going to get a royalty. So that's really tough because I... When I talk about my compass, my strongest compass is what's best for a patient. Always has been.

I'm a doctor. So I want you to have the best doctors who put in that catheter but if the best doctor made that catheter and has a gain from that, I find that really hard. And that's where I think very careful systems have to be built up so that you don't harm the patient by not letting the person who can put that in, but the patient has to have their eyes wide open to all of what those complex could entail. That's the trickiest part of that. Let's go right in the back. Yeah. I have a question. If you could talk a little bit more about the risks involved in either a position that you've been in. In the sense that, as you mentioned, life science, you're kind of playing with the people's lives. So, when you're talking about ten year in horizon, multibillion dollar project, with impact on potential human beings, how do you come up with a cost benefit analysis and resource outpatient for choosing what to invest in when the stakes aren't just financial but, you know, common lives or researcher's potential entire career.

Right. Right. So the question is about how do you balance this risk of adverse outcomes long after you have a drug approved. There's a few principles that I think you can use that I like because they align business' interest and patient's interest. And so, I've always use this principle as aspects of how you do product development that are really clear and actionable. And the principles are as follows: one is, all this concern, appropriate concern about side effects diminishes in the phase of patients who are in a harm's way. So there's always been a principle on oncology that you treat patient who has metastatic disease, disease that spread in part because those patients have a disease that today you can't cure. So when you're balancing benefit and risk, if the patient who you're treating, early on in that drugs life before you understand its side effect, has an incurable disease, the stakes for that patient are so high that they're going to die that you can accept those side effects. I mean, that's just the way it is and the reality is that patients have told me and I think they're right, "You're over protecting me from side effects. I'm the patient.

I've got six months to live. You protect me from a drug that might have side effects in five years?" I guess the pearl there is listen to patients, never stop listening to patients. They're always going to give you a better answer than your own mind because they're in harm's way. So if it is possible to treat patients who are staring a bad outcome in the face, that is the best experimental system because they don't have options. So I think that is absolutely the most important thing. The second thing, and I think this is where academia needs to innovate, and we must, must, must, must address this. As I mentioned, my career was heavily influenced by the HIV/AIDS epidemic, having been at UCSF and travel to Africa. I mean, it's sort of a horrible thing to say but true. When I went to Uganda, the first trip back to UCSF was six months later, all my patients had died. I went back to the AIDS clinic and all my patients had died when I came back six months later.

I mean, that's just shocking. What changed that? So just in a few years that wasn't a death sentence. There was a surrogate marker for outcomes in HIV/AIDS. You could measure viral load in the patient's blood. So again, this benefit-risk, if you could markedly decrease the viral load and you could measure that in a month, you knew right away you are helping the patient. That's why I like infectious diseases, the readout is so fast. So anything you can do to read out something that predicts the future benefit early, again, allows you to balance that risk and benefit. So we need better markers in diseases like obesity, Type 2 diabetes, cardiovascular, cancer that tell us, "Gee, here's what's going to happen to this patient ten years down the line with their cancer," so that we can balance that benefit with the risk. We don't have those tools today. How about right here.

Yeah. So you talked a little bit about how at UCSF, you're trying to merge the life sciences with the technical and sort of... That's one of the things that I've always seen with healthcare that's been a huge problem, is that the entire process from being diagnosed to being treated and cared for has always been you have to go through an expensive specialist. Who, not only do they expect to be paid for the fact that they have gone, trained for ten years or however long, but that also makes it unable that these people are able to work in developing parts of the world. So as medicine goes for, how much do you think places like UCSF and this research and development is going to be focused on more pumping out the most specialized people that we can or pumping out things that allow people who maybe aren't specialized, but to diagnose, to treat. And this cost effective ways of approaching problems versus throwing brilliant people at a problem, I guess. So that is a fantastic question. The question really gets to what do we do with the healthcare system. I like the description of our healthcare system. It's neither caring nor a system.

So it is not where we need to be. One of the things I'm really excited about is the opportunity we have in medicine to make some changes in things that are actually not that complicated. And so what you're describing is something that increasingly we're all talking about which is on two ends of the spectrum. So on one of the spectrum, you have 30 million more Americans who hopefully will have insurance between now and 2014, so that everyone has access to healthcare. And I'm definitely a believer in access to healthcare as a right. If we have 30 million more Americans, we need the healthcare providers to provide very basic services and yet we do two things that don't make sense. One you mentioned, which is we throw high-end remedies on low-end problems. So, we might have a provider who cares for somebody who has skills that allow them to do brain surgery and there you're front end provider. That may not makes sense if you don't need brain surgery. So, we need to have the skills set match up with the problem.

The other thing is increasingly, we're asking ourselves, "Did that problem or that issue need a caregiver?" Then, why do go to the doctor to get your blood pressure checked? Couldn't that happen at home where you're not scared and just drove and found a parking space so your blood pressures up? We do things in medicine that are not sensible. So, on your basic primary care family medicine, community medicine, we need to drive towards simpler remedies and more cost effective remedies. On the other end of care, we need to...And I'm grossly over-simplifying but we need to sort out our two aspects. One is something that people call on-if you're physician, you kind of cringe at this but-a focus factory. So a focus factory means that if, God forbid, you do need neurosurgery, are you at the place, are you at the academic medical center where that guy or that gal just did ten of those surgeries this week? Or did they last do one ten years ago? So for those very high-end procedures, can we minimize the number of places that do those so they get very, very good at them? And then, are we really thinking about end-of-life care? We spend 80% of the money in the last couple years of life not helping someone die in ways that are more humane often. So how do we think about end-of-life care? And when we have that discussion, people worry about death panels and not saving their love one, but we have to have that hard discussion about end-of-life care and what we spend on end-of-life care, in whom should we do the heroics. If you look there's a very nice article by a physician named Atul Gawande in the New Yorker just last week about chronic illness and how so often the cost of health in chronic illness are driven by social issues, substance abuse, homelessness, lack of a job, lack of access. So thinking about what is the root cause of the problems we're trying to solve with modern medical care, they may not be amenable to the remedies we're using. So, all of that is part of some of the pilots that are going to happen as part of healthcare reform between now and 2014. Sue, we do one more.

Right here. So when we talk about innovation here at Stanford, we talk about collaboration between life sciences and medicine and business and engineering and law. And given that UCSF is only a life sciences campus, what's your vision for fostering inovation in this collaborative way there? So that is a fantastic question and one of the things that I think we have organized for ourselves is an ability to interact with other campuses. So, global health is really a very good example. I would

throw in to what you mentioned, agriculture, really increasingly important in global health. So we put together global health initiatives with Davis, with UC-Berkeley, with Santa Cruz, with UCLA so that we're going across the UC campuses. And specifically in health, there's an organization loosely called UC Health, and that is the five campuses at UC that have academic medical centers. UC Health are working together on innovations that start at how we do contracting, how we deliver care, how we do purchasing together but end up looking at some of the things that I was just talking about in healthcare reform and how we can collaborate across the five UC Health Sciences campuses to solve medical problems. We also now have a joint bio-engineering program with UC-Berkeley. So increasingly when it involves law and engineering and life sciences, we collaborate with Berkeley who also don't have a medical school.

So it's a good collaboration actually. They're pretty close and you can go under the bridge which is essential. So the bridge is an impediment but we increasingly collaborate across with Berkeley. All right, thank you so much. Join me. Thank you.