



Stanford eCorner

A Tearful Tale of Biodesign [Entire Talk]

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November 16, 2016

Video URL: <http://ecorner.stanford.edu/videos/4689/A-Tearful-Tale-of-Biodesign-Entire-Talk>

Michael Ackermann, CEO of a med-tech startup that created a tear-stimulation device for those with dry-eye disease, explains how acquisition by a global pharmaceutical giant is helping him achieve his goal of reaching as many patients as possible. Ackermann, a graduate of the Stanford Byers Center for Biodesign, also discusses why big tech companies have yet to disrupt healthcare and how that translates into big opportunities for entrepreneurs.



Transcript

(applause) - Well, very well, thank you very much for the kind introduction and how are we doing out there? Anybody who has an election hangover, this is an election free zone. So today, we're going to talk about something fun. We're going to talk about innovation in healthcare. And in part, through telling you the story of Oculeve, the company that I co-founded out of Stanford to treat dry eye disease and it won't be a surprise to most of you, if anyone has read the news in the last couple of years, you know that healthcare is changing right? So, we're seeing increased expenses, there's a lot of things that are changing in the environment as a result of that, it may even be hitting your own pocketbook, but what I thought we would do, is just look at the change by the numbers. So the graph on the left here shows healthcare spending as a fraction of our GDP over the last 50 years. You'll see that it's going up and to the right. And 2014, the last year for which data was available from the government, we spent 17.5 percent of the GDP. 17.5 percent of the entire gross domestic product on healthcare spending and it's done three trillion dollars. And we're feeling it, right? We starting to hear about pressure on prices, we're starting to hear about healthcare premiums going up and some of that cost gets shifted to the patients. And we're hearing about it in terms of consolidation in the industry.

Another phenomenon that's happening. So the plot on the right actually shows the fraction of Americans that are insured, right? And you'll notice in the last couple of years, largely because of the Affordable Care Act, there's a very large increase in the number of Americans that are insured, as well. I do believe that even under a Trump presidency, there's going to be some impetus to provide a program for driving insurance amongst the population. So, what's happening is that we're running out of room for growth in healthcare spending. We have more people, who need to be treated and we're all starting to feel a pinch, right? And so, we're feeling it as patients and we're certainly feeling it in the industry. So our government also makes available the expenditure in terms of where those three trillion dollars is going, so let's take a look. So more than half of that three trillion dollars is going to hospitals, it's going to doctors and to clinics. About nine percent of it's going to drug companies. About three percent of it is going to medical device companies and then, a series of other things, including I think notably, a seven percent that actually just goes literally to support the infrastructure of the insurance companies and the federal Medicare and Medicaid. And every slice in this pie is feeling it.

So there is drive on every single one of these to start becoming more efficient and we can see that in terms of consolidation and so, what's happening on the private practices are being brought up and consolidated into hospitals. We see hospitals that largely had been independent for a long period of time, consolidating into hospital systems, both regional and national. And we're seeing consolidation of the drug companies. We're seeing consolidation in the insurance companies and in the device companies, as well. And all of this, is in an effort to drive more efficiency in the system. So, let's look on another dimension. So now we know where the dollars are being spent, what is it being spent on? So according to the CDC, it's down to 86 percent of

this three trillion dollars is being spent on management of chronic diseases and so that chronic diseases include things like heart disease and diabetes, some types of cancer, but it also includes things like dry eye disease, which is what our company was focused on and something that I'll tell you more about. And so what does all this mean? Well, something that's sending a little bit of a shutter through the industry is frankly, that there's going to be a higher bar, right? In terms of, providing efficient treatment and so that's the technologies that are more expensive for incremental benefit, frankly, probably aren't going to get in the marketplace anymore, at least not as easily. So that's the bad news, but what's the good news? Is that there's a heck of a lot of opportunity out there. So you have this three trillion dollar marketplace, this enormous industry that is literally, changing under our feet right now and there's huge opportunity because someone has to be an agent for that change, right? So tremendous opportunity in this consolidation, as well.

So, one of the things and we'll talk about it that it's actually hindered some of this change and change by technology is that there's very separate groups, right, and you go get your broken leg fixed by one physician, you get your eyes fixed someplace else and your primary care physician, who may have referred you to these places, can't even look up in their medical records to see exactly how that went, right? So that consolidation actually can be a real opportunity as well, particularly on the information technology side. And then, layered on all this is really a tremendous opportunity in chronic disease. And so, providing better or frankly, just more efficient ways to care for chronic disease. So logos of our friends and neighbors here in Silicon Valley, right? We're here, we're used to all this technology coming in and completely transforming a marketplace, right? And it's the way that we connect, it's the way that we buy goods, the way that we get around, the way that we interface with the world. And we're used to these big technologies coming in and making a real difference, right? But here, healthcare 17.5 percent of gross domestic product and none of those logos are a healthcare company, right? And it's been very, very slow to be converted by big technology, so why is that the case? Well, there's a few reasons. So one is that there's a very complex network of consumers. So if you're Amazon, it's very clear who your consumer is, it's the person whose buying the goods, right? Well, in healthcare, it's a little different. You got the patient, who we usually typically think about. This is someone who is either being diagnosed or being treated, but frankly, a lot of the time, they're not even the one whose making the decision as to which product to use, right? The decisions oftentimes, being made or at least, heavily influenced by a healthcare practitioner. This is the doctors, the nurses, the technicians.

These healthcare providers very typically operate in a hospital or a hospital system and so that hospital also has tremendous decision making ability over what products are used for the patients and by the practitioners within their system. So you got another decision maker. And frankly, none of these people are actually paying for any of it, right? It's all paid for by an insurance company or it's paid for by the federal government, Medicare and Medicaid. So yet another customer that has to decide that this is the right technology to use. It's also a highly regulated industry, so you also have to satisfy the FDA and they have their own sets of needs and requirements. And it's also an industry that's very heavily influenced by the professional medical societies. So these are societies that provide guidance to the practicing public, what's the best practice to use and to not use and they also have a very heavily influence over the payer system, as well. So what products actually ultimately, end up getting paid for and make the list. So okay, why don't we have Amazon of healthcare. Well, one of the reasons is this very complex network of consumers.

Why else, well, it's also a very conservative industry by nature, right, and that's actually probably justified. So we are talking about people's health. If we make bad decisions, there are very real and bad consequences for it, so every physician before they start practicing, they take the Hippocratic Oath and they vow to first do no harm and that attitude actually, pervades not only in the physician community, but the FDA and industry as well, so it's everyone wants to make sure that things are safe. Another thing is that medical innovation oftentimes, relies on new science. And sometimes, new science happens a lot slower than new software. So it could be a tough thing to go there. We have a distributed provider system and meaning, as I mentioned before, one place for your knee and another place for your eyes, another place for your heart. Same thing with the payer system with all these different payers all over the place and then, also, finally both ethical and legal privacy concerns, as well. So maybe it's no wonder why we haven't seen this big enormous splash, right? We haven't seen someone come in and just completely, transform this healthcare space. But what really excites me and why I think it should really excite you and I'm hoping that a few of you in the audience will want to take a good hard look at healthcare because frankly, this is really a once in a career type shift or opportunity.

What we are starting to see is a lot of little splashes. And we're going to start seeing a heck of a lot more than that. So coming into one disease space at a time, coming and attacking one inefficiency at a time and this is really going to start snowballing. So for the rest of today, I'm going to talk to you a little bit about Oculeve, this company that I spun out of Stanford with some others. This is the device that we developed for treating dry eye disease. Take a good look at it because it's not the device that we started with and so, that's all part of the story too. And so Biodesign, it's this center, over in the Clark Center, so right down Campus Drive and it's just a really neat space and so, the plug there, is that they also have an undergraduate and graduate course sequence in addition to this fellowship that I was a part of. So I would encourage you to take a look at it. And what they've done is they've taken this philosophy that I think has really pervaded a lot of Silicon Valley in the last couple of decades that also was developed here, this empathy based design, so this is by David Kelley and Tom Kelley, other folks at

the D school here at Stanford, really formalized this process and the idea is that by going and understanding the consumer, right, and gaining empathy for them, then you can really understand what their needs are and develop a solution for that need. In the healthcare space, Paul Yock and Josh Makower, the founding faculty of Biodesign, put that same principle and brought it to healthcare and in healthcare again, the consumer is a little more complex, you have this network, but the same principle turns out to be really powerful.

So the mantra there is a great clinical need is the DNA of a great solution. In healthcare, for a long time, we've talked about bench to bedside and this is where you've got this great scientific idea and we have a way we're going to now convert this into clinical practice, right? And that's really been the one of the mainstays of innovation in healthcare and frankly, it's still very important, right? The catch is you have to have a great scientific innovation in order for that to work, right? So unlike me, I certainly didn't. I came into Biodesign with three other people in our group of four, I was quite literally, assigned to go innovate in ophthalmology, right? I didn't know anything about the eyeball. I knew I had two and they were important to me. But frankly, I was a little disappointed. I was like, well, this thing's the size of a ping pong ball. What could possibly be going on in there? I'm sure everything's already fixed and fortunately, I was very naive. But what Biodesign teaches and again, it's this empathy based design is this really bedside to bench to bedside. So you go back, unless you already have happened to be sitting on this great and important discovery. You can go back and say hey look, what are the needs, right? And we know that there's this huge driving force in healthcare, in terms of efficiency.

It can really be the seat and the tidal wave for a lot of that, as well. So here we are, this is our group of four. Brandon was an engineer, Victor McCray's a surgeon and Garrett Smith was an engineer and scientist and again, we were assigned ophthalmology to go innovate something. One of my favorite things about Stanford, I'm sure you guys are experiencing this already, but this is just incredible because you have a question about something and the world's complete expert is literally two buildings down, right? So you just go knock on the door and you talk to somebody. We actually got very fortunate that there was a very passionate and innovative MBA student, who also happened to be an ophthalmologist and in fact, a specialist in dry eyes. She had spent additional trainings, specifically studying this and so we partnered up with her, Vandana Jain, as well. So as part of this Biodesign program, there's this immersion, right? So first you got to go get the empathy, right? So we spent four weeks and we literally, just watched clinical care. So we sat around, we goofed off a little bit, this is Garrett here, empathizing by sitting in the patient's chair, but we watched patients come in and we watched physicians do surgery, we watched what the issues were and I was just amazed, frankly, by coming in with a very naive beginner's mind of how quickly it is that you can start identifying issues, identifying inefficiencies, identifying opportunities. So in the short three to four weeks, we identified some 347 clinical needs. We went through a filtering process that was primarily, looking at what is a real clinical problem, what represents a bonafide commercial opportunity and ended up with dry eye disease and if you're a little bit like me, the first time I heard of dry eye, I was like dry eye disease, really, is this a real problem? Turns out it is, so if you were watching television last night, you may have even seen some commercials for some dry eye drugs and that's because eight percent of the population has dry eye, primarily post menopausal women and it ranges from something that can be a bit of a nuisance to something that frankly, is very debilitating.

So it actually, a really phenomenal public health impact in a big market and so, our real insight here what we came up with and what kind of allowed us to hang on to something that was kind of special, is that at the time and I think frankly still, people think about dry eye in terms of this very complex system that's going on. There's 40 boxes in this model and there's 80 arrows pointing around all the things that are happening and frankly, what we said is okay, but if you boil it down, there's really only two boxes and two arrows, okay? The body is not making enough of the tear and the tear is very important. It helps your cornea stay clear, so you can see, nourishes the eye and if you're not making enough of it or some part of it, then, the eye becomes dry and inflamed and the more inflamed it becomes, the less able your body is able to make this tear and kind of round and round we go in this cycle. And what's interesting is when we layered the pharmaceutical industry on top of this and the device industry, which frankly, there's very little happening in, all of the people that were focusing on innovation for the last 20 years, things in the market place, things in the pipeline, everything was focused in that left box, okay? Everybody was attacking inflammation and no one, not for 20 years, had someone gone and actively looked at restoring these natural constituents of the tear film, so that along with just frankly, some muscle in terms of going in and understanding the anatomy and what's going on, we kind of had this aha moment, where we said okay, look, maybe we can use electrical stimulation to activate the nerves, to innervate these structures and get the body to make its own tear again. Okay, so now we got this great idea, right, where we use electrical stimulation, we're going to activate this nerve, we got this really cool thing and that, we can't believe nobody's thought of and what our thought was that we were going to directly activate the lacrimal gland and we were going to do something, literally, this is an image that we showed some doctors that we were going to take this pacemaker like device, we were going to take a wire, we were going to run it under the skin up the neck and then plug this very thin wire, of course, that we were going to then plug into the orbiter, the eye socket and the reception was not good. So the first doctor we showed just about passed out and said, whatever you do, don't show the patients and so we obliterated it and we brought this one in and the thought was okay, look, now we're going to move to a much smaller device and maybe the issue was the whole neck thing, whatever. We'll move it back here and then, we'll run the wire up, right? Well, very similar response and he was like, okay, I don't think you guys are getting it. And the first time that we started getting nodding heads was when I brought this

in. In the upper right, what you see is a little piece of black plastic with some green modeling clay on it. That was our first prototype for what ultimately, became the implant that's sitting below it.

And the idea here was that it was an injectable implant that would sit next to the lacrimal gland, the gland that makes the majority of this tear and it was going to act like a little pacemaker and again, having looked at where we ended up, something must have gone sideways with this one, right? Because we didn't end up with it and I'll tell you about that. But so now, we're kind of going into the second year here at Stanford, okay? Identified some new partners. So Jim Loudin was a post doc in the physics department. Mark Blumenkranz and Daniel Palanker, faculty here at Stanford and we were able to raise some money. So Bases was mentioned earlier. We were fortunate enough to get \$25,000 check from the Bases competition, put a little bit of money in the bank, we were able to use that to get some venture back seed capital and do some early work. So I'm going to take a pause here because what I'm telling you sounds like a very linear story right? We go out, we're going to go into clinic, find some deeds, we got this great deed, now we're going to go and come up with a solution to it, that's terrific, now we're just go raise some money and then, that'll all work out and move forward. And retrospectively, you can draw a straight line through every one of those points, right? But what you don't see is there's a lot of other points on that too. And so, this was actually a very difficult time. This was a stressful time.

There was a group, where we're trying to figure out do we want to be entrepreneurs or do we want to go work for a company, right? And so, what I'd like to do is talk a little bit about managing personal risk and something that for those of you who are interested in entrepreneurship, who are sitting in this room, I think is very relevant and part of the reason that I'm bringing it up is because oftentimes, I see young entrepreneurs taking, what I believe anyway, to be probably unreasonable risk. Sometimes going all in on something that's very, very high risk. So at least want to pose a couple of thoughts and then, kind of swing back the other way in terms of what you can do to manage that risk as an individual. Alright, so you're thinking, do I want to go out, be this entrepreneur or do I want to go and perhaps, work for one, work for another company. And so, I'm going to give you some unsolicited advice, but I think hopefully, it'll be helpful for you. So the first thing is, consider your opportunity cost, right, so I'm seeing a lot of young faces in the room, which makes me think that the vast majority of you are students, right, so you wouldn't be here if you weren't very capable and didn't have a lot of opportunity, right? So by jumping in, going all in on something, you really are, there's a cost to that, so you're giving up something that might be there and just to kind of plug that side. Now that I've been at Allergan for a year and a half, I realize there frankly, are a lot of opportunities in big companies, right? So there's really tremendous opportunity to make impact because these companies are actually, already in the market place and they're there with the customers. There's a lot of opportunity to innovate within these companies because they have resources and also, personal growth because you're being taught by people who do something really well. On the other hand, if you have something that's interesting, if it's something that you really have the bug, you have good people around you and getting encouragement from it, then give it a go. It's something that, you sort of describe it as, it's 90 percent of the time, we're living the dream and 10 percent of the time, it's sheer misery and there's nothing in between, but that's a pretty decent trade off there.

But what I would recommend is to the extent possible, hedge, so if you're thinking about starting a company, you're in a really great position right now because you're at Stanford or perhaps, you're working someplace else in a similar situation. This is the best incubator in the world, right? It's the best incubator for you, in particular, not only because of all the resources that are here and all the people that are here, but also because if something doesn't work out, right, a year later and this thing goes belly up, your next employer all they know is that you were a really involved and interested student at Stanford, who had this great side project of something going on, is really creative, right? And if instead, you kind of go all in on something and it doesn't work out, well then, the story is a little bit more complex. So alright, so enough of that. What I will do is kind of talk to you about what we did and for me and for our group, we set a threshold and said, okay look, we're coming up on this two year mark, we're about to be released slash punted from campus, right? So what happens then and do we want to set a threshold because frankly, I was applying for jobs at the same time, right, I didn't know what was going to happen and cultivating relationships because it was uncertain. And for us, our threshold was really raising a bonafide Series A and I'm not saying that this should be the same threshold for everyone because every story is different, but the reasons that we chose this is primarily, because if we were able to get real money into the company, then we could set, have a much higher probability of success, right? And that's because there's capital, that's because we've got better people around the table, people who are experienced and know what they're doing and frankly, on the worst case side, it is a really great experience, right? You're getting experience managing a project, managing individuals, et cetera. So in our case, what we needed was basically, data showing that the device works and fortunately, in our case, it did. So we did some early animal work and actually, some even early clinical work and we were able to raise a pretty solid Series A from three venture firms, Kleiner Perkins, NEA and Versant Ventures. So at that point, we were really off to the races and it was really a very fun time, moved into a kind of a shoebox of an office, especially when you need lab space, 1,800 feet. We started packing in, at some point, we're growing and we had literally, little cubbies set up on the conference table, people were working in the copy room and it was a lot of fun. So we built an implant, it ran our first clinical trial.

And I kind of told you the end of the story on this one a little bit and that sometimes, the first idea isn't always the best one,

right? And so we build this implant, we get in there, we treat 40 patients and fortunately, safety was very, very good, no one got hurt, but some patients got efficacy and some of them didn't, right, so it was working out really well for some, it was not working out quite as well for others and simultaneously, we're feeling this healthcare environment changing under our feet, much faster than we thought that it could, right? So here we are, we're building an implantable device, it's a procedure, it's invasive, it's going to take a very long time to get approved and actually, get onto the market, so especially, looking out and saying five years from now, what's the healthcare environment going to look like? Is this really what we should be focusing on? It's also expensive for the payers, expensive for the patients and so fortunately, this coincided with us actually having a really nice insight and what we realized is actually, that our best performing patients, despite having an implant on one side, actually were getting tearing on both eyes. Now the reason that's really exciting is because it turns out those two eyes aren't connected, right? The only way they're connected is through the brain, which tell us that we're actually activating reflex. So we got to thinking instead, okay, is there another way we can activate a reflex to make this happen and actually, Jim Loudin and I were down in Mexico eating fish tacos, there's Jim eating said, fish tacos right there and had this idea of actually, activating the nose. So inside of the walls of the office, we had this affectionately called the reflex, the wasabi reflex. So everybody in the room, whose ever put too much wasabi on your sushi, kind of back draft it in your nose, right? You know exactly what this reflex is, you got a bunch of tears pouring down your face. Now what you may not know is that actually, for every single person in this room right now, this reflex is actually active right now, driving your tearing, so unless you have a cold or allergies, you're breathing through your nose, so every breath that we take, both in and out, very gently activates the same nerve that the wasabi does and drives a third of your tear production right now and so it turns out that if you activate it, then it can be a really nice and effective thing for dry eye patients, so not only, were we able to get the better efficacy from it, but it really fit within this archetype of what we were looking for for the healthcare environment as well. It was something that was non-invasive and better for the patients, it's cheaper for the payers, cheaper for the patients, provided a quote, practice building opportunity, which means, the doctor can actually provide this product out of their office, provide a revenue source, where they're getting cut in other places and also, provides a really nice opportunity to leverage information technology with a blue tooth enabled device. So here's the device, it has two components to it. The blue part is a rechargeable, electrical stimulator device. There's a little disposable that goes on top and that disposable has some hydrogel, that allows it a kind of connection to the nose and as I mentioned, it's blue tooth capable and has a digital companion app and what's really nice about this is now we can leverage the technology that this valley has developed for everything else and introducing it into ophthalmology, where it's never been there before.

And what it allows us to do, it allows both the patient, but very importantly, the physician to track how the patient's doing. What it also does, is dry eyes environmental disease, so we can use geolocation, weather data and say, alright, using humidity and wind and temperature, et cetera, is this going to be a good dry eye day or a bad dry eye day, something very important to these patients. And with frankly, something as simple as being able to leverage your smart device to order refills, right? In the same way that we order anything else and it checked all the boxes, right? So it's better for the patient, better for the healthcare provider, we pulled it out of the hospital system, so there's no surgical procedure there, it's cheaper for the payers, it's less invasive and less risky and therefore, cleaner path through the FDA and fortunately, has been very well-received by the societies. So I will show you a quick video here, you get to see this thing in action, so what you're looking at before I start it, this is a close up of someone's eye, the bulls-eye rings are a function of the device and the light source that's on there, so it's not anything funky going on with the patient and what you'll look at, is the very lower lid margin there. Okay and so, what you'll see, the patient just started using the device, within about 10 seconds are so, you'll see a pretty dramatic increase in the tear link there, the tear production level and what's also was really fun for us as it turns out, I mentioned that there's different components in the tear coming from different organs and actually, this reflex activates all of them, where our first device was actually going after one and that's something that's actually very important from a clinical perspective, as well. So this is healthcare, so we do clinical trials. We've completed seven trials to date, treated almost seven hundred patients and the device is currently sitting with the FDA right now, so fingers crossed, we're hoping we can launch this in the first half of next year. So as mentioned before that we were acquired by Allergan in August of last year. I do want to touch on that as well. So in addition to the obvious in terms of providing return for the shareholders, most importantly, Allergan creates this enormous lever for us, right? So if we're a very small company and we're trying to go out and treat patients that are not only all over the United States, but frankly, all over the planet, right, it's really hard, you got to one rep at a time.

It's something that Facebook advertising alone isn't going to take care of because you do have this complex network, you need a healthcare provider to actually, ultimately, prescribe that device. And Allergan, they're the world leader in the space right now, right, they have sales representatives in the offices of 23,000 eye care professionals in the US alone, that's almost all of them, right? And what a just really tremendous opportunity for us to be able to make a really meaningful impact on public health in a very short order of time. I did also just want to touch on it, now that I've actually spent some time in a big company and just reflect on it a little bit, as well, sort of in line with some other things we've talked about. In addition to kind of this management of risk that I think is important, certainly to some of our staff and I've also learned a lot, right? I'm there, I'm working at a place, we're about to launch a product and we're going to launch it in a world class way, right? And learning from people, who are very, very good at this. People who are skilled in manufacturing, learning how to do that and I think that's also true for our staff, as well, being able to come in and really learn from people, who are frankly, some of the best in the business.

And particularly, at some of these later stage parts of the product cycle and again, making this opportunity to make impact. Now one of the things that has been really fun about this, is that there's money there, right? I mentioned that when you're in the startup, you have confidence that there's going to be the next check, if you're doing the right things, but frankly, there's a lot of uncertainty there and when you're at a profitable business, there's a lot of resources and so, actually within our group, we have two pipeline products that weren't there when we started and actually, some really innovative folks within our group have developed two new technology ideas and they're up and running and it's really nice to be in a place, where that can happen and I think that to echo sort of the opportunity for entrepreneurship, as well, just relaying that that can actually happen in a big company. So I'm going to leave you there. What I am going to say is that this is just an amazing time in healthcare, literally, almost 20 percent of our entire economy, right, that is largely untouched by the types of technologies that this 20 mile radius has been transforming the world with and it's a really exciting time to be there. There's a lot of opportunity, not only to come in and move the market with share, but frankly, to really do a great thing for our community and for our country, we need it.

It's getting really expensive. We're having a hard time keeping up with it and so, I hope that some of you guys will take a look at healthcare and maybe, take a look at the Biodesign courses, as well. So with that, thank you very much. (applause) Yeah of course. Alright, so sure. - [Audience] So when you were finishing the Biodesign program, you said your threshold at getting a Series A, but you could be essentially, trying to get to that threshold for a while, when did you know it was, you were going to pursue that capital versus pursuing a company, I'm guessing there was a time crunch there, as well? - Yeah, so the question was, it's not like you can kind of magically time when you're going to get the financing and so the threshold was the Series A and how do you sort of time that and especially with respect to other opportunities that might be happening. And it's not easy, right? You're constantly reading the tea leaves. You're constantly trying to push out your hedge opportunities and saying, oh, we've got a few more months, things are really exciting about this, et cetera and then also frankly, just really digging in and trying to drive people to closing at the A. I think one thing that has certainly happened and what I would recommend is to the extent possible, when you're in a great position to do that, is I would talk to somebody whose experienced at fundraising. I think the way that I would go and raise a Series A now, is just so different than the way that I raised it the first time.

I think that there's a lot of things that you can do to really not only garner interest and excitement, but frankly, manage a process because everybody talks about running a competitive process and how you try to get multiple term sheets and really get the best value for a company et cetera, but the reality is, people don't reach the end at the same time, unless you really drive them to do that and that's something that I didn't actually learn until raising later money. - [Audience] So you have this innovative digital device. It's taking in a ton of data. Can you talk about if you're using data in data science to make both the device better technically and also, from a business model perspective? - Yeah, so the question is basically, how are we leveraging the digital aspect of the product and how is that driving both the business model, but also the technical side, as well. So I think just as data enables a lot of other things, it's not valuable in and of itself per say, but it can really be a great enabler. In our case, we use it, again to enable care, so it's something that allows physicians to check in, they can look at a portal, see how patients are doing and Mrs. Jones, I'm sorry you're not feeling good, but maybe it's not a big surprise because you haven't been using your treatment. Again, also in terms of providing direct value to the patient from looking at the environment and other things that directly impact dry eye. But where I think things can be actually incredibly powerful from a business perspective is that in lots of industries, the customer relationship is the relationship with the customer is very direct. So Google knows more about me than I know about me because I do everything on Google.

But in the healthcare space, when someone writes a prescription for drugs, you don't even know who has the script, right? You literally don't even, that person's completely anonymous. And so what that does, it makes it really hard to know what could be making things better for that patient, how do you make patients more compliant, and how do you impact care in a meaningful way there. I think this is something that's really powerful with a technology like this, is that you have that direct link, you have that direct customer relationship and you can nudge them, right, and you can say, look, you're not using it the way that it should or the doctor can nudge them and say, look, you're not using it the way you should and et cetera so. - [Audience] So one major difference between a software startup and a medical technology startup is all the regulations, so there's the FDA, there's CMS, can you comment on how the landscape is now or maybe how you're trying to streamline the process to get faster from product creation to market? - Yeah, so the question was, the big difference between software and the healthcare is that it's highly regulated, right? And then, in addition to the regulation to even be able to get onto the market, you have this entire reimbursement side that has to be covered too, right? So not only does it have to be approved, but somebody has to agree that they're going to pay for it and so, how does that impact things and how are things potentially changing? So what I would say is that in some ways, it's very tempting to think about those things as barriers because frankly, they are barriers, right? You got to go through a lot to do that and you have to have knowledge of this system, right? You have to understand what this regulation thing is all about to be able to get a product onto the market and then, you have to understand what this reimbursement thing is all about to get there. What I'll tell you is it's a great thing. Here I am, I'm a total neophyte, just spun this thing out of Stanford just four years ago and I don't have some high school or a Pali High coming up with a competitive version of our product, that's going to launch immediately after, right? There's some complexity there, but there's an incredible network of people in this valley and beyond that understand the nuance and frankly, it's not rocket science, right? So it doesn't take a lot to understand it, you just have to be able to get that understanding and then, play by the rule and once you get on the other

side actually, it's really a tremendous barrier that actually ends up being very protective. And there are things that are working to make it go faster, but inherently, they're long processes, right? But I think that's part of the trade off. The markets are equally as large, even a very tiny fraction of a three trillion dollar market is still can be a multi-billion dollar market, right? It's still enormous markets and so, there's really enormous opportunity. But you're not competing with, you have intellectual property, you have FDA, you have reimbursement barriers that really prevent competitors from coming into the space. Sure? - [Audience] So you spoke about when moving to Allergan, how that provided you with more resources and stuff, I'm kind of curious on a leadership level, it went from you and your partners kind of running your own company, your own team to now being part of much, much bigger organization, how did that work out for you? - Yeah, so the question's about leadership and going from something that's a very small company and starting off in a real partnership level to even in a growing startup frankly, and then, transitioning to now, a company with some 25,000 employees in it, what is that like and what does that mean and frankly, it's actually very different.

One of the things that I've actually really valued about my learning experience at Allergan, it's just a very different type of leadership, right? When you're going and even in the startup phase, where it's you and some buddies around a table, everybody's involved in every decision, right? You're sitting there and you're making calls and you're going off and doing things. You don't have to have any real structure from a management perspective. And as that grows, you have to both evolve leadership and management and there's a distinction there. So leadership in terms of setting vision and setting culture and that really has to start becoming real as you start having more than just a few people around the table and that also, is leadership in a startup, where you're setting the vision, so our vision was we wanted to be the world leader in dry eye. It's got to be ambitious, right? Because you're going out there and you're trying to change the world and if you're not shooting for that world-changing thing, then you're never going to get there. And setting an environment that's a good place to work for others, et cetera. But also setting up a management system that is able to kind of tolerate and make functional a larger increasing group of people and so, we've gone from having no management system, there was a white board and three people around a table making calls to having a formal management system in a small private operating company to now, in this huge major space organization, right? So there's people in other parts of the organization that are making really important calls on what we're doing, the leadership is actually, previously, it was my team that was reporting to me and then, actually, out to the world, in terms of being an evangelist for the company. And now actually, a lot of my effort is spent internally. I spend a lot of time with internal sales, right? So I'm going in and selling other parts of the organization on what we're doing and really have to influence people that aren't reporting to me oftentimes and it's actually, it requires a different style and you have to motivate people in different ways and so, it has been different, but frankly, it's part of the fun of this experience. Anybody else? - [Audience] I have a question, Michael.

So in hindsight now, besides the funding, was there another indication that you had that you were onto something compelling. In hindsight, besides just the fact that you had an external VC invest in you, was there another milestone that you think, when you knew you were onto something big? - Well, so the question is, what were the other signals that we were onto something important, as opposed to just this funding event, right? And frankly, they're the same signals that you get for whether or not you're onto a right life partner or you're onto the right anything else you do in your life and that's, are people around you excited about it, are you getting positive signals from it or are you getting negative signals, right? And frankly, it doesn't, it's not just this and or, but it evolves and there's constantly negative signals, but can you keep evolving that? And iterating very, very quickly to where people, there's momentum in that and it's actually, people are getting more and more excited or is it something where it's like okay, I'll take this meeting because you're at Stanford and you're a professor at the courtesy of sitting down with you for 20 minutes or is it something where people are they sit in, they're like, oh my gosh, actually, this is really interesting, you should think about this, this, this. So that's a lot of it. - [Audience] One more. - [Michael] Yeah. - [Audience] And so is a new administration and a potential change to the Affordable Care Act, something that a prospective med technology entrepreneur should factor in, if they're thinking about building in that tech fund. - Yeah, so the question is, what does Trump mean for healthcare, right? And what does Trump mean for anything, I don't know. So there's frankly, it's a big question because it's, I think there's a lot of uncertainty around what the agenda will be and I think there's uncertainty, not only in terms of communication, but I think that frankly, there's uncertainty within the administration as to what the position is going to be and there has been talk of either completely dismantling or meaningfully changing the Affordable Care Act that certainly will impact healthcare. I think there's also been talk from the Trump campaign about maintaining some sort of system that promotes high insurance percentages within the country, as well. What I do think is that fundamentally, I think that the same problems are going to be the same problems. The same things that are driving all this tremendous change.

We're kind of tapping out of this 17, 18 percent of GDP and even if it goes to 19 or something, it's still an issue and whether or not we're dealing with a 95 percent insured population or an 85 percent insured population, it seems to be the same sorts of things, but it may have some impact on how acute it is or is not. - [Audience] How is this applied and how long does it stay in and also, while sneezing if you insert something on the nose, can you stimulate sneezing? - Yeah, so the question is, how does the device work, right, and does it activate sneezing? And actually, I would say the first time or two you use it, patients often do sneeze because you've got something in your nose, you're activating these nerves, the same thing that if you were to get something stuck up there, your body might try to sneeze. It's really those first couple of times that activates that, but you

saw in the video, it's literally, 10 seconds are so. Most patients use it twice a day. So you leave it in your bathroom, use it in the morning, use it in the evening and then, basically use it until they get the effect. - [Audience] What are the side effects? Does your nose drip or what are the things you were fighting against? What are the things that came up? - Yeah, so the question is what are the side effects and what are some of the things from a clinical perspective that were we up against and frankly, beyond kind of the occasional sneeze that happens, one of the things that's interesting actually, is that the tears actually, drain into your nose. That's actually, part of the function of this entire reflex. So those tears wash out the wasabi and if you're watching a really sad movie or a sad election perhaps, and then, you really cry, you start sniffing, right, and that sniffing is a function of those tears being in the nose and so there is some sniffing that can occur, particularly, if you really give yourself a good dose, but one thing we've been extremely, I'm trying to think of, I think the other side effect that occasionally happens, is that if patients have a really, really dry nose, and you place something in your nose, then you might get a little bit of spotting of blood, but one of the things that's been really great about this particular technology is that it is so low risk and it's something that from a trial perspective, the FDA formally designated as a non-significant risk product and it's so great because now, we can actually reach a much wider fraction, of those 30 million people, who have dry eye because it is so low risk, yet effective, unlike the procedural treatment that we had. - [Audience] When you were in the process of conserving the biomedical industry and looking for inefficiencies, how did you narrow it down from the hundreds of problems that you found to just one? It seems like it would be difficult to choose one problem. - Yeah, so the question is, we had these 300 and some odd needs, how did we kind of narrow it down to one? It seems like it must have been difficult.

The answer, yes it is and so, really there's a few things. We applied kind of a high level filter of what is a genuine clinical problem and what has commercial potential and what I mean by that and I think this is actually, quite true, well beyond healthcare, that's you got to look at what is the potential value, what is the market potential of this product and is the investment that's required to get there to actually get this out there, commensurate with that opportunity, right? So if you're going to have to go through and healthcare projects aren't cheap, right? I think getting a medical device to market on average, is 70 to 100 million bucks, right? So those are big dollars and if you can't be convinced that at the end of that, you're going to have hundreds of millions, if not billions of dollars in revenue, then it's really a tough call to make in terms of being able to garner the investment on the front end to do it. Now on the other hand, if you're going to be making something that is less intensive in terms of price, you're making a surgical instrument, something like that, then maybe, it's hundreds of thousands or whatever it is to get there, then the market opportunity doesn't have to be the same either. We rightly or wrongly, we were looking for a big opportunity and that was one of our filters and then frankly, we were looking at these different problems and dry eye was the one where we had the idea of how to fix it, so, that was part of it too, yes? - [Audience] Do you see opportunities to apply some of the learnings on the design side and the medical device experience to therapeutics in a world of molecules in a more traditional pharma sense. - Yeah, so the question is, is there anything that can be applied from this device side to the pharma side? The short answer is yes, I'm actually very excited about biopharma right now and there's a lot of reasons, but some of the challenges on the pricing side don't exist to the same degree anyway, obviously, it's been a political football, but to the same degree on the drug side as they do on the device side and I think there is that opportunity, but I think it tends to be a certain blend, a certain type of therapeutics. So for example, we actually had a drug program at Oculeve and we spun it out into another company and that company is an independent operating company right now and that was a pharmaceutical that rather than going through and having this really key insight, we've realized that there's this receptor on this cell that nobody else realized was there and we've gone through and designed a molecule to go in there and tag that receptor. Instead, we said actually look, you could possibly activate this same pathway, the same nasal pathway frankly, using a pharmaceutical spray, as well and so, we went through a pretty organized process of actually going down, screening molecules, but we were screening molecules that were already out in the market place. Somebody else had already taken them to a certain level and it turns out that the ideal molecule was actually sitting in a company that was going defunct, the molecule, they'd run it through phase two trials, it was very, very safe, but didn't treat gastroparesis and so, we bought it off them and so yes, I think you can still use those same techniques, but I think it's maybe not on as much on the discovery side, but certainly on the development side. Okay, thanks guys. (applause)