

# P5 Health Ventures

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## Opening Remarks

### **David L. Eigen / Co-Manager P5 Health Ventures:**

I got a call two years ago from my mother, on August 2014, saying, "Bruce wants you to call." I said, "Okay," and so I called Bruce. Bruce said to me, "I fund all this research, I do all this work ..." I'm paraphrasing. "I have all this knowledge and it's not getting translated into treatments. It's not getting moved into the population. There is tremendous opportunity out there and it's not being taken advantage of."

That's how this started, and I hate to use the term but a cabal started between Terry, Bruce, Aaron and myself to figure out how could we accelerate and make more accessible things that can help people. That can help them now. Not the miracle drugs that will go through FDA approval eight or 10 years from now. Rather, the things that can incrementally grow over time, because things evolve that will seem like revolutionary, but are really just evolutionary. Things like Google took years until they were big. Everything seems overnight until you look back at their history and it wasn't. What we have now which is really tremendous, from the Googles of the world, from the Apples, from the AT&Ts is this massive infrastructure. Hundreds of billions, trillions of dollars that are put in, that lay the ground work that we can all take advantage of.

Aaron and I are going to try to do a minimum of speaking, but you'll hear from companies today that are at what I would call the cutting edge. One company in particular Biorealize is very much at the cutting edge but they're simplifying and delivering things to the masses in ways that previously could not be done. A lot of these things, all the companies here today I think in hindsight you will think there will be researchers out there, when they hear it, they'll say, "Well, why didn't I think of that?" Those are usually the best kind. It means that everyone else's perspective was off. We're here; obviously, you're here for a handful of reasons. You're here to learn; you're here to learn about science. You may be here to learn what we're doing. You may be curious to get more information to invest.

Whatever it is, we're interested in healing people and finding solutions that will change healthcare for the better, that will be less invasive, that will be more preventive without feeling like you have a chore to do, and that will overall change the culture of healthcare. With that, I'd actually like you to get a feel for some of the people involved.

### **Aaron J. Moskowitz / Co-Manager P5 Health Ventures:**

We've got David's background on where he came in, but we first started talking two years ago. I've been working with Terry for the last 14 years on a nonprofit. Very much interested in helping new ideas take root in hospitals, academic, medical centers, patient populations and that's through the nonprofit BREF (Biomedical Research and Education Foundation), when David mentioned that he had spoken to my father about opportunities that are languishing in these centers and in health and they could be mobilized and put into use today, I was: "Yes, yes. I'm seeing tons of great things." We're seeing tons of really smart people that are just at the brink of making it into a larger population, helping more people. It seemed almost a no-brainer.

We came up with the idea of P5. Let's go through a couple of quick slides before I formally introduce Terry. Just to give you a little bit of our mission and why we're here. There's a disclaimer [Slide 2]: that's not one of the slides I was excited about. The P5 Health Ventures ... Again we're looking at this, we're building companies. [Slide 3] That's really what's happening, and to do that, we set up a fund. [Slide 4] It is The P5 Health Venture Fund which is the vehicle; we'll explain how that works. We did it as a team. There's a whole group of people here who have been having a lot of fun talking nerdy science. Talking about health and what it means for people and we'll get to everybody soon. With that, I'll introduce Terry, whom I have known for 14 or so years now.

**Terry Fadem / Advisor:**

Right now I'm a senior fellow in the William and Phyllis Mack Institute for Innovation Management at the Wharton school. Before that, I was director of Corporate Research for Penn Medicine. Before that, I did a bunch of startup companies and before that, I was the director of global business development for the DuPont Corporation. A small but growing company on the banks of Delaware. One of the reasons I'm interested in this, and what got me started in this is because what we do at the Mack Center. I'm a senior fellow there. It means I'm an older guy who they don't really know what to do with. They call me senior, and I don't object to that anymore.

What happens is that I see and I work with academics who study what it takes for innovation to be a success. My role then as a former industry guy, is to figure out how to translate that into action. One of the venues that I've chosen is P5. What I see on the academic side, a lot of students really young MBA Scientists who have great ideas about new businesses, new technology, you'll hear about some of them today. Where do they go, how do they get it translated into action. A lot of the stuff sits on the shelf, literally sits on the shelf, for years or gets abandoned because they don't know what to do, or where to take it. My view is how can I make the link between what we learn in academics and what we can do in the real world market place, sooner, faster and better and that's my role with P5 and I make that link for us.

My history is I've done it myself. Not everything worked. I'll admit to that. When they work, they work well and it's a difficult job and someone has to help people make the connections and that's what I'm doing with P5. I will tell you one brief story to give myself a little bit of credibility for this. Bruce Moskowitz, whom I did not know 17 years ago, called me up one day with an idea. His idea was, "G-whiz I don't know how to get knew information, new technology information into the hands of an internist like me." He used a word in front of internist which I will not repeat. The word was "dumb." You all know Bruce, there's no such thing "dumb" about Bruce, but in anyway way he was looking at new technology, and said how do I gain a better understanding of that technology to make use of it in the practice for my patients.

After our phone call, he and I got together on the phone, literally, we hadn't met and we translated that idea into the Biomedical Research and Education Foundation, a real thing. It took us a couple of days to do it, and from that we became friends and it became obvious to us that we could translate ideas into reality without much work on our part. We find young guys like David and Aaron to do that work and then everything works smoothly because they've got the energy and the time to do this. We became committed to finding better ways of translating

ideas into healthcare in the practice of medicine. That's my link to Bruce and how all this got started 16 years ago. I've known Bruce a little longer than Aaron.

Real quick, these are the people on our advisory board. [Slide 5] I'm going to let them introduce themselves and tell you who they are and why they're here and the important thing for them is there link into helping us do this translational work. New science, new technology and new ideas into practice.

**Dan Beiting, PhD / Advisor:**

My name is Dan Beiting. I'm faculty at the University of Pennsylvania, so across and down the street from the famous Wharton School. I've been there for about 10 years at Penn and about three and a half years now on my current faculty position. I thought what I'd do, just sort of start off is set the stage for the kind of work that I do and I think it will help sort of introduce in concept and in science some of the companies you're going to hear from today and some of the real core aspects of what P5 Health Ventures is really trying to achieve. My training is in microbiology and immunology and that's important because as a microbiologist all of my training was about things that caused disease. Things that make people really sick. We don't have to look far to find out about these things. You turn on the news right now. We're hearing a lot about Zika.

Two years ago, it was an Ebola outbreak that started in West Africa. 10 years ago it was West Nile Virus outbreak. There's always a new bug out there that's really scary, but what's changed is that microbiology has learned that the world around us is not just scary bugs, there's actually this entire ecosystem of microorganisms. Bacteria, viruses, other organisms called archaea that live in and on our bodies and that actually are covering surfaces of the built environment that we work and live in. This sort of unseen dark matter, microbial dark matter, over the last 10 years has received a lot of attention. What's become really clear if we just sort of cut through all the boring laboratory science, is that these microorganisms don't make us sick. You can take that one step further and say they're actually important for keeping us healthy.

This has really fundamentally changed the way we think about microbiology and it's also changing the way we think about disease because now when we think about the reason we go from being healthy one week to sick the next, we think about genetics, maybe playing a role. We think about this vague thing called environment. Now more and more we're appreciating that one big piece of this environment that tips the scales towards disease is this microbial environment that lives in and on us and that lives on the surfaces that we interact with. This is called the microbiome. You're going to hear a little bit about that today. The other thing I just want to touch on before I pass the mic off, is that there's one question that you should probably wonder at this point.

Which is well you told me this is microbial dark matter, how do we study it if we can't see it? That's where I think places like veterinary schools become really pivotal. At veterinary schools we talk a lot about something called "One Health". It's something that every veterinarian and veterinary researcher understands but I'm always surprised at how few human physicians really get this concept. It's really simple. It's the idea the environment, our pets and agricultural animals and human health are intimately connected. You can't disassociate them. If we really

care about public health in general, we need to think about environmental health, think about the health of our animals and think about our own health, they're all connected.

At a veterinary school, one of the things I bring to the table for P5 Health Ventures is we look at animal diseases as a really close parallel to human disease. They develop spontaneously. Pets develop inflammatory bowel disease, actually completely spontaneously. You name it. You name a disease and I can give you an example of a parallel disease that develops in animals. That gives us a context to understand disease and how it develops, to intervene and to extend what we learn from that into human medicine and we get the win-win situation of improving the health of our animals which I'm very passionate about. About animals, about pets and growing up on a farm, about agriculture. I'm sure many of you have pets, but it also lets us care a lot about human health in the process.

That's sort of a 30,000 foot overview of some of the themes I think that I care a lot about. I run a research lab. A lot of the tools I use to do this work involves genomics and big data. One of the things that I look forward to doing is any of the companies that come through interact with P5 when they need those kinds of analytic tools, that's what we're here to help them with. To give them the tools to understand the microbiome and health and disease.

**Kristi Clay, DC / Advisor:**

Good afternoon. My name is Dr. Kristi Clay. About 25 years ago I graduated from Chiropractic College, and one of the things that I realized was the concept of innate intelligence in Chiropractic School is very paramount. It's something that the entire profession of chiropractic has been built on. That is a concept that relates to the body as a whole, and cannot be taken apart in pieces. The idea is that if you remove the obstacles from the body, the body will make every effort as a living organism to heal or to right itself to find its imbalances and bring itself back to right. Whether that means an illness or a deficiency state. A vitamin or a mineral deficiency state, or it means a mechanical problem with the body that maybe interfering with the brain's ability to communicate with the rest of the body via the spinal cord or the immune system.

I went on and became very interested in nutrition. I was certified in nutrition and then went on beyond that for a three-year post-graduate degree and got my diplomat in nutrition. I started a complementary medical center that had acupuncture, chiropractic, had a naturopath. I had massage therapist, I had chi gong, and Tai chi. We all learned to find different levels of support for people. What I found was that someone who may not do very well with acupuncture and resisted acupuncture because they didn't like needles for example, might have a completely different experience with deep tissue massage or soft tissue massage or a naturopath. It became something that was very, very important in my community as people became more educated about how these alternative modalities worked together.

I had the personal opportunity then to see what that would look like when my son was diagnosed with leukemia at three-years-old. The day that he was diagnosed, I actually was sitting in Stanford. He was treated at Stanford for three years. I'm from the Bay Area. During that time, the best that I felt like I could give him, was to support him through that process without having his chemotherapy process stopped. One of the things that happened, particularly for children's leukemia is that you're given something called a roadmap and that

roadmap is literally every day of the next three years of your child's life is scripted out. The only time that you defer or detour from that roadmap, is if the child immune system fails and they cannot handle any more chemotherapy.

Trying to stand back and look at a three-year-old and find the best way to accelerate his process through a three-year, very long, what seemed to me a very long process at the time. Was to be able to support him in a way that kept him from opportunistic infections. That kept him from deficiency states that kept him from gaining or losing too much weight. That kept him from cachexia, all of the things that we usually associate with chemotherapy. I started using German biological medicine, homeopathic medicine and a lot of lymphatic drainage protocols with him, and watched him flourish actually as he went through chemotherapy and one of the most complicating problems for me actually, was not watching him be sick in a hospital bed, but it was actually watching him ... Trying to keep him from pulling out his mediport. He would jump, he would jump on the bed!

He had so much energy as we were going through this process that my biggest problem was how to manage a three-year old and keep him busy in a hospital room. It was sort of not an amusing time but there were interesting things that came up during that process. I would watch his physicians walk by his door in a long sea of rounds that they would do every day, and I would watch them back up and go, "Is his chemotherapy on? Okay he seems to be doing great." They would go on to the next room. This was not the experience for the other children that were there as I'm sure you can imagine a lot of these children were very, very, very ill and have a lot of secondary complications. Bacterial infections, hair loss, weight loss. They didn't want to eat.

My passion for finding nutrition and supporting cancer patients through that has grown. I now sit on an advisory board for a camp called Camp Okizu which is in San Francisco and it's for children surviving life threatening illnesses and I write the nutritional protocols for their camp, in order to try to increase their knowledge. I want these kids to be survivors and the best value that I can give them is to know how to manage their bodies going forward with as much information as they possibly can. I don't want them eating fruit loops and I don't want them eating high fructose corn syrup when they're at greater risk than the regular population. That's sort of became my passion and I think that's why David and Aaron reached out to me.

That's my role for P5, I'm also an advisor for Primal. Emily's invited me to join her advisory board as a clinical advisor and I'm very proud of that. Thank you Emily, and I'm happy to be here.

**Terry Fadem:**

There are two other advisors, one is here and I'll save him for last, and the other is Katie Schmitz. I'll speak about just momentarily. The story that was told about her son bouncing up and down and having all this energy, is a good one to remember because we have Katy Schmitz who's another one of our advisors who is an exercise physiologist. Very entrepreneurial and she's realized that not only do you need to get treated, but you need to know how to act when you're being treated. You need exercises. You need some type of a

program in order to deal with the therapies and treatments and diagnostics that you're getting. That's her role. [Note: Kathryn Schmitz could not attend due to other professional demands as she was leading a conference.]

Then I want to introduce Dr. Moskowitz who I have claimed to have known for 17 years. Most of you have known him for longer. Who's another advisor. Bruce you want to talk about Brent?

**Bruce Moskowitz /Advisor:**

Brent Bauer, it's an interesting story at the Mayo Clinic. He is in charge of a city block. The city block that he's in charge of is the Wellness Center. When you go to the Mayo Clinic, the old physical was just your examination and your test, but this actually evaluates you to keep you in your spot, to keep you in top notch condition for ever. They are very innovative; they come up with a lot of strategies for wellness. He's a phenomenal asset to this board; he knows every aspect of the Mayo Clinic and interacts with all the research scientist, so it's a phenomenal position. [Note: Due to his work schedule, Dr. Bauer was due to arrive the day of the presentation but was indefinitely caught at O'Hare airport and missed the presentation.]

**Aaron J. Moskowitz:**

If you want to get back to a little bit on this diverse group and they all have a variety of expertise, not just siloed into one idea of what medicine is. That's sort of how David and I have been thinking about medicine when we first started talking and what does it mean to be healthy, and how can we impact our own health? [Slide 6] How we take care of ourselves, how we eat, the way we treat ourselves mentally and of course making sure we can move. These are things that we could do day to day, they are very accessible and they impact all aspects of our health.

This is a very holistic, integrative approach to medicine and health and wellness and it manifests itself in a variety of different ways. Obviously what we eat, to look at our stomachs, in our mouths, how those things interact with our heart. We look at how our mental health is affected by outside and inside and how we feel pain and of course mobility and being able to move and working really at our physical fitness; it's both reflective and how we explain ourselves. Of course that's just one component; what does that mean in practice? We first look at the individual, at the center of our circle is a little bit of our graphic. [Slide 7]

We have the diagnostics, digital health, things that help define who we are and where we are health-wise. Moving out, we go back to the three pillars that we've just discussed, so we have things that we can eat, mental health, exercise. Then the outer circle is really how that gets to individuals. We want to make sure all of these ways to translate ideas and new ways of treatment make it to the individual. We are interested in making sure all these things happen in the near term; we are not looking 100 years out; we are not looking for single miracle cures. These have to be accessible both in terms of application and in time.

Of course we are talking about medicine which is a large market. [Slide 8] It is a bunch of large markets; we cut it up but there is no way around it, it's big, we need to remain focused on what we can tackle and those very important parts.

[Slide 9] We developed our investment approach and philosophy. We want to make sure that things are accessible to everybody; we want to make sure that we are looking at big areas; healthcare is large, but make sure our opportunities are large and the companies could service them. A lot of different aspects of health, the platforms that are applied widely.

Make sure that doctors would use them; make sure patients would use them. This is important; otherwise they are gimmicks, toys, things that aren't used meaningfully. We expect things to change quickly; we've all seen the influence of the internet and a variety of infrastructure, digital infrastructure that David mentioned earlier and this is going to happen quicker, so we have to be looking ahead; it's very important. We think patients and individuals will take more control of their health; they are the key decider; they know when to go to the doctor; they know when to eat healthier; they know when to exercise. Of course when we look at any of these opportunities, we have to look down first to ensure that we are doing the right thing, looking at the right companies. Evaluating the risk on capital and also our time and working well with our team. To elaborate a little bit more on that, I'm actually going to let David do that, we have some slides on how we'll be investing and looking at opportunities.

**David L. Eigen:**

[Slide 10] Okay, so this is the exciting part before we get you to the companies. I've spent a lot of years in managing portfolios and public equities and the one thing I always looked at was risk. I am incredibly paranoid about risk, especially in early stage healthcare where the risks are significant. Having a very cohesive strategy to approach risk and how do you take down your risk ahead of time before you make the investment and then after you've made the investment. These are the components of our investment strategy.

[Slide 11] First, how do we source? As you heard in the beginning, Bruce, Aaron and Terry had significant, not just access, but interaction on a regular basis with major medical institutions and we expect that that will continue. We've got several relationships with NYU, with Tufts, PENN [all schools] and a host of other, Mayo and other institutions that we will be going through their portfolios on a regular basis and a preferred basis. I also came with a history of investing in other private equity funds and deals.

We have ties in the New York Community and Boston Community and the Silicon Valley Community and elsewhere and we are actually going to spend a lot of time looking East of the Mississippi, where valuations are more rational and where there is a lot of innovation, where people have what I will call a healthy chip on their shoulder. Again, how Biorealize is here through Dan Beiting; Kristi has really come up with a host of things. She is long-time friends with one of our other [not on the board of] advisors; that advisor is another physiology professor at Stanford who sees every metabolic and every pulmonary device that comes through on the west coast or here or invented pretty much anywhere in the world comes through her office.

The next thing is the integrative health community, which we actually believe that it's still a relatively small, but rapidly growing area where every major medical center in the world now has a facility. Brent Bauer runs the integrative medicine clinic at Mayo and founded it. What I would argue is those places are still relatively behind where individual practitioners are because they can't go there at a big institution until something is proven out. That area is growing very rapidly and what technology is doing is taking diagnostics and taking tests that

costs thousands of dollars that are rapidly dropping to \$150, \$20, \$10, \$5; of course a hospital may charge you \$500, but it's only costing them less and less.

Then again, corporate partnerships, Terry has a lot of relationships; we all do; and then to me, there is nothing like being on the road, knowing people, meeting people like you. I know we all make donations; I know professors; I know researchers; I know other businessmen that are doing interesting things and having that network, what we call ecosystem, where everyone keeps adding value to each other is something that is essentially core; you will hear me talk about that again. Then of course we know all the accelerators and innovations programs and incubators and doing all the things that you have to do.

[Slide 12] What are the attributes of a portfolio company and this is when we bring this together; we've gone back and forth on what are the attributes of a company and how do you manage risk? They are very intertwined. We look for platforms, things like Primal, which you'll hear about in a little bit, which has a way of manipulating, engineering biofilms in the body, and you will understand that better, but for those of you who don't understand, every bacteria talks to each other and protects each other by forming whatever I guess you would otherwise call mucus, but we call biofilms.

Her first application is the mouth, but that technology works on your hair, on your underarm; it works on a dog; it works on this floor; it works on the subway that you don't want to touch that post; it works everywhere. [note: the first formula was designed for strep but also appears to work on staph. Testing has started.]

You look for a clear path to market; so, we don't want to be in something that's going to be five, ten years from now and we don't know what the competition is going to look like, and we don't know if it'll ever get engineered and put there. We look for solutions to real problems.

One thing we've heard consistently, when you talk to say this professor [advisor] on the west coast is that "I get all these people with the technology looking for someone to use it" as opposed to we look for people who have had a problem and found a solution as a result of knowing what the problem is first. Again, large market opportunity. We look for a high caliber management team or people who are problem solvers; who know how to get things done, who are easy to work with and who are driven to succeed. The science and technology, if you look at the first two investments we've made, you'll see that we go through great hoops to understand that technology, it's protection, it's intellectual property.

[Slide 12 & 13] The competitive viability, here today in this day and age, you don't know where the competition is coming from. You may have a perfectly good solution; you may think your antibiotic is great, but there may be a probiotic or there maybe something totally different, like what Emily has created at Primal that can completely usurp the market. By the way, this solution, you can do it for pennies and it doesn't require hundreds of millions of dollars to bring it to market. Then we look at our ability to add value. If we can add value and we can be involved, we have to be able to talk to companies to notify them that we think they've made a mistake, they are pivoting in the wrong direction.

We also want to, again, lower risk; we want to be able to bring all the resources to bear. One of the problems I have with any fund is that it has a life to it and we think that we are getting involved with companies that we may never want to sell. Of course that's a good problem to

have, but that time may come; but either way, we need to know that there is someone out there that values this company more than we do.

Due diligence I don't want to spend much time on this but it's very obvious; we are out there; we have a scientific advisory board; so we are always one phone call away from not one but three, five, ten experts. Whatever we need to get to the bottom and understand the markets [and science].

We look through everything, market acceptance is very important and as Aaron talked about before, would a patient use it, will a doctor prescribe it, who will stay on them whatever this product is to use it. We look at the legal risks and intellectual electoral property risk. As Terry always says intellectual property is only as valuable as the war chest you have [to defend it].

Actually, very quickly on Primal. Terry, you worked at DuPont. I like to say in new business development, but global M&A; he's bought and sold bio-tech companies, developing intellectual property capabilities that PENN has, on the corporate side.

We got Terry together and Gerry [Casey], a friend of the family, who is the former general counsel of Pepsi and we took a look at Primal. We said first of all there is a strategy, which I'll let Emily talk about. How do we protect it? Do we file a patent? If we file a patent, are we putting it out there so everyone can see what we are doing and can they copy it? Gerry, actually from Pepsi, was the trustee for the formula; he had it in a safe in his office and do we protect it that way? We look at all different ways. Again risk of obsolescence.

Regulation is another thing that I did get a question from someone and it was an email; "I just want to know are you in Obama Care's target?" What I would argue is we are not touching anything that is where congress is going to pull one of our CEOs in front of them. We are not even looking ... Obviously the companies need to get bigger. We are looking at the companies that democratize healthcare and make them more accessible.

[Slide 14] The portfolio itself will be 10 to 12 companies, early rounds we're looking at Seed and Series A. Seed rounds, I don't think there is a situation where we are not going to lead a Seed round, at an early stage. First investment, half a million to a million dollars. Series A is a little more advance for them, I can always talk to anyone who wants to understand that part better. These are a little more advanced companies, typically. We just invested in Cohero who you'll hear from; they just took in nine million dollars.

Then the other factors just in terms of managing risks. Of our three pillars, we won't go more than 40% in any one, we won't go more than 10% of funding in a single round. Companies need to perform and we are not going to throw money at things and then hope they perform. We are going to put money in on a methodical basis; when they hit milestones, and they get momentum, we'll commit more capital.

[Slide 15] Risk management; as I talked about milestones and incremental investing, if you look at the top, like big opportunities. Looking at small opportunities, usually the small markets and they are very hard to compete; they take the same amount of work. We are at an age now where technology has become so pervasive that we would actually argue a lot of these really big companies, because they get very kludgy, are actually the larger risks. If you want to put your money in an index fund with a lot of big corporations in a time of disruption like there is

right now, I would argue and I still do this as a hobby, my bigger fear is for the bigger companies ... The irony of Warren Buffett investing in IBM, right as the company has borrowed a ton of money to go buy back its own stock, when everything other than Watson is falling apart, is indicative to me of the fall.

That means in the ashes of that fall will rise companies like this. You seeing it in the internet and basic technology, and we really believe that healthcare in next. Again, I feel like I'm repeating myself, but we obsess over risk management and we're sensitive to evaluation, we get a preferred return. We make sure we are the first money out. If the company doesn't work and it's a platform and there is intellectual property, we believe that we can get our money out.

[Slide 16] Adding value, I think is fairly obvious. We have board positions, we are active, again we bring our business network. [by example] Katie Schmitz can run tests in her lab for certain companies that we're looking at, and a host of other labs that we are looking that will do the same. Dan is running genetic screening in his own lab for Primal. He is overseeing screening for new compounds for Emily's company through another group at PENN and we'll continue to do those kinds of things.

I'm a nut about capital allocation, return on capital, you put money towards something, what's the return? And then brand building: That's something that I, actually back in college, worked for someone who invented the term "corporate voice," and in the advertising industry, he's a very famous man; I'm still regularly in touch with him. For me, a brand, in the case of Primal we are probably going to something like "Primal Inside", like "Intel Inside" and understanding what that does to add value and that it creates residual value as well. That brings us to the companies, because I think the best way to learn is through examples. [Slide 17 - List of Companies]

# Cohero

<http://www.coherohealth.com/video>

## **Melissa Manice, PhD:**

Sorry that I have to be remote today, but thank you so much for taking the time to listening. We are excited to have P5 part of our team in this recent capital raise that we closed about 2 weeks ago after our series A. I thought I'd spend a bit of time grounding the Cohero platform in the use case and for the patient and provider in need for a solution like this. My PhD is in pulmonary medicine and bioinformatics. I'm the CEO and cofounder of Cohero and I really built Cohero out of the desire to build and scale a solution rather than spending a lifetime studying a very well documented and costly problem in circles in the pulmonary space.

The patients that we treat, the two of the very pain points are lack of compliance to their daily medication, and then the lack of transparency around how they are responding to therapy which lung function is the most critical indicator. We really are bringing respiratory care into the 21st century, taking advantage of incredible advancements in digital technology infrastructure and ultimately I think what has been a catalyst for us is this move towards interoperability. The platform allows you to really integrate natively into work flows like EMRs. We've done this very successfully.

Our two core assets, being these two proprietary devices consisting of course the ability to track and remind proactively allow patient to self-manage, but then also reducing ultimately something that David really mentioned, reducing the cost of specialty care and point of care diagnostics while we're taking something that's currently restricted to a specialty practice being that pulmonary function testing device. It currently costs about \$25,000 and actually having gone through the FDA, our mobile spirometer is actually FDA cleared, and we were able to show that we were within 2% margin of error of a clinic based system. It's completely mobile and costs about \$200 to make.

What we've done to date that we are very proud of is to really focus heavily on getting incredible sort of user traction, but also just as importantly to focus on clinical validation. You really feel that this is something that as your selling, for us, our core sort of business models to sell B2B, to firms and benefits managers, provider systems, pharma et cetera. Having that clinical sort of evidence base has been critical to us. We deploy the full platform in a series of clinical trials at Mt. Saini. We are able to demonstrate a significant improvement in outcomes through looking at avoidance of hospitalizations or reduction in hospitalization of patients as an end point. Show the significant increase in medication compliance to their daily medication and therefore decrease dependence on rescue medication. Then continue to basically replicate.

We've gone before the FDA as we're trying to actually to get the entire platform reimbursed as sort of a dedicated re-imburement code. Through that, they have reviewed our clinical trials protocols for expanded RCTs that we've expanded across an additional 5 clinical sites. An incredible strategic advisor to us, to date, has been Blue Cross Blue Shield. Their venture arm was an early investor of ours and their chief medical officer has been very active in helping us

sort of build the case for re-imburement, of which we think will assist in hitting that inflection point.

In advance of really having our own dedicated codes, we've generated about 1.2 million in booked revenue this year alone. Q4 of this year was our fully commercially ready year, and so we're very proud to be covering about 8,000 patient lives in advance of even having had a full commercial launch. The series A raise, was really intended to allow for a response to incredible sort of commercial interest, and in particular allow for expansion of some dedicated pharma programs for our embedded smart inhaler.

I think with that I'd love to take questions. I know that David was hoping that I mentioned kind of where we are commercially that we have about 24 active customers. Representing, again, about 8,000 patient lives and 1.2 million in revenue which are health systems and EBM programs. With that thank you so much for your time and I'd love to take questions.

**Male:** What's the primary distribution channel for platform and the device?

**Melissa Manice:**

That's a great question, so the two most fundamental distribution channels for us are providers - and that includes large health systems, small practices, ACOs - and then pharma. Pharma, I should mention, and I guess without the privilege of having the slides, I could circulate them after. We spent the past two years developing and integrating our technology into the actual drug delivery systems, so into the inhaler actuator and partnered with PressPart which is the largest manufacturer of actuators and canisters globally; they sell about 500 million a year to pharma. What that's allowed us to do is to really have an incredible entry into pharma opportunities and which they're really switching for many reasons their sort of analogue devices into sort of smart drug delivery systems.

Our first awarded contract represents 20 million devices a year. That's something that we were awarded actually as we're kicking off our series A and is expected to launch by end of year. Those represents the sort of 2 core channels of which we obviously see payers as really also being an important player in the provider space.

# Strategies for Bone Reconstruction

[P5HV - November 2016 Presentation - Paulo Coelho.pdf](#)

## **Paulo Coelho / NYU:**

Kind of difficult to even start talking about how all of this actually crystallized as you're going to see over five minutes eight minutes of conversation that a lot of work has been performed. We are happy and afraid at the same time that we are so ahead of the game, that we may be able to deliver some academic research. While in reality what we want to do is to use all of the resources that we have add some more in order to deliver something that would be a strategy for bone construction through three dimensional printing.

I work at NYU. I work at the college of dentistry. I am a dentist by training, oral surgeon. I'm an engineer as well and I work also at the department of plastic surgery which is led by Doctor Eduardo Rodriguez, and he's an integral part of what I'm going to be showing.

The work that we do in academia is interesting because you end up doing academic research [Slide 2]. Most of the scientists believe that academic research is going to ultimately translate into a product, regardless of how good actually the deliverable may be.

We're not that romantic so we know that we're going to need help even though we are funded by three ... actually we have the distinction of being funded by three different institutes from the national institutes of health and by the department of defense for reconstructive surgery. Everything that we do especially between Doctor Rodriguez and I happens to be translational so we are not only working on figuring out how to grow bone fast, but also we're working towards models that will rapidly enable us to translate this to the clinic provided that everything we promised the different institutes actually is delivered.

The motivation [Slide 3] I think that everybody here understands that once a bone is either fractured or gone, it turns out to be a problem; so in US we're talking about 900,000 hospitalizations due to fractures. When you think about some congenital malformations, if you think about cleft lip and pallet in craniosynostosis which is fusion of the cranial bones, and some of these kids actually have to be operated as early as days after birth, we're talking 1 to 600 and 1 to 2,000 to 2,500 in the US. We're talking about over 1 million grafting procedures annually, and even though the technology and surgical approach has improved substantially over last year, we still have 5 to 10% impaired healing due to known union and need for further grafting procedures. That's the civilian population, that's the day to day routine that you end up getting.

If you're talking about the military personnel, that is much more problematic. This is the general population where if necessary you can always autograft; you can take a piece of bone with vasculature of muscle and graft it somewhere else for reconstruction. Some of the military personnel ... I took all the "as my surgeon colleagues would say" the gruesome pictures of this type of incidents that appear in military personnel. At times we don't even have anywhere to pull bone from, so you have to have a different strategy in order to reconstruct them. When you

have anywhere to pull bone from to harvest bone from those are usually infected because you're dealing with multiple injuries at the same time. High incidents for infections further challenging healing, so reconstructing military personnel is much more difficult relative to the civilian population.

What would be ideal? The ideal would be a synthetic material [Slide 4], so it would avoid us having to harvest another bone from the body in order to do the reconstruction, and that has to be biocompatible. It has to be osteoconductive or inductive, and by that I mean the material will have to have the ability to guide bone regrowth into its own structure. Ideally degradable so you have nothing to harvest after the bone is regenerated so you don't have to go in and do a second procedure. And ideally, this will be customizable which has recently been enabled by additive manufacturing which is nothing but 3D printing

That was something that we used to use about 5 years ago as the holy grail of bone reconstruction through any sort of method. Today, this is something that we already have, and we just need to take it to the next level when it comes to gaining throughput of the technology. That would be a personalized reconstructive surgery leading to vascularized bone with original morphology. In regular words, it would mean you come in, you're hurt, we reprint the missing segment that you may need of your bone, we go in, we do the surgery. We don't have to harvest it from another site so it avoids another surgery. Then it ultimately grows bone that is viable that has the same properties that your old bone had and you don't have a material in the end of the day there. It goes away. That will be the ultimate goal, when we got kind of lucky when we were doing research over the last three years.

One of the things that we do relatively well and we're ahead of the curve on this which is 3D printing [Slide 5]. What we're doing here [Slide 6] we're printing a bio-active ceramic which is bio compatible and osteoconductive so it favors bone growth. The interesting part of it is that we can take a CT of a patient, subtract the factor, figure out how the surgical approach is going to be, and print the part that needs to be implanted. We know that this is going to be successful given the number of pre-clinical experiments that we have conducted over the years. As soon as we started pulling 3D printing in there, we have been able to recruit even high school kids to spend time with us over there.

That's the only gruesome one, not that bad, and basically what we did we reconstructed a piece of lung bone which is a critical segment. A critical segment is a segment that will never heal on its own unless you graft it from ... You harvest bone from another place and close this gap. We printed the bio active scaffold, and as you can see there's perfect fit and fill here for this particular pre-clinical model. We allowed it to heal for 4 weeks or 8 weeks, 12 weeks and 24 weeks in hope of getting vascularized bone with mechanical properties of the contralateral ... Or let's put it this way the old bone that you had.

Translating this, this is 24 weeks healing [Slide 7] and the dark component that you see here is the scaffold. This used to be continuous as you saw on the previous slide this construct. The RAD component happens to be bone. We were very successful in recreating bone; we were also able to recreate the bone marrow component of it which is very important for a variety of physiological reasons. Here is the computerized tomography of bone itself so we recuperated or we regenerated the original morphology of bone and at the same time something that was continuous turns out to be non-continuous. That's why we were able to get funding from reconstruction of congenital malformations of kids that are born with these malformations,

because we know that we can rapidly regenerate bone and at the same time the scaffold that we're using has gone away so the growth is actually not precluded when the kids are growing.

In a nutshell, we got all the properties that we were looking forward to having right here in the very first experiment. Then Doctor Rodriguez and I have always been skeptical about everything, so we thought that the long bone segmental defect was actually a big problem until we started to look into the cranial muscular facial defects [Slide 8]. The problem with this guy here: we have the mandible, which is a moveable bone, which you have to regenerate and still a lot of movement for it. Most of the cranial facial bones happened to be very thin, and they're sandwiched by other tissues that may get in the way whenever we're trying to reconstruct them.

In short we ran very challenging models of very thin bone of what would be analogue to a cancerous action of half of your mandible for obviously therapeutic reasons and then you have to somehow reconstruct this [Slide 9]. As you can see there's perfect fit and fill by the scaffold right there and only eight weeks after healing these defects are considered extremely challenging. We have a phenomenal amount of bone actually within the scaffold right there. Here is a total chunk taken out of the mandible we have been able to actually regenerate the whole thing. We are definitely on the right track, and as we see as the future we need to do private development relay the research. All the grants that we have from the National Institutes of health and the department of defense.

They will be phenomenal as a tool for us to figure out and maximize bone healing so we can deliver a product over the next years that is going to be highly successful. Obviously we will expand to other areas [Slide 10] such as dentistry, veterinary medicine. One of the applications I did not mention, which is a natural here, would be orthopedic surgery for spinal. Any type of spinal problem; from spinal fusion to compressive fractures and so on; that's actually as we see the low hanging fruit, given how challenging the defects that we have been able to regenerate work relative to this. We are already talking to the FDA with respect to initial approval. Clinical trials are obviously in our future, and hopefully as a scientist and as someone who has had the privilege of receiving that much federal funding is to give the tax payer back what I have promised them over the next 5 to 10 years.

Then I'll move on into another problem we'll solve something else and let's hope that this will turn into a nice company that will deliver a healthy or health alternatives to those in need.

**David Eigen:**

To date, we have made two investments; one was Cohero which you heard, but because of my own health history and I've had some gut issues and this is part of what drove me, the biggest impetus was starting with my own health when I was young. Then family members [illnesses] and so the microbiome is my biggest area of interest... Of course I went to every other doctor over the years [who all had the same things to say].... I finally found someone with Emily's approach and I have to say something. I think the lowest hanging fruit in medicine today and in all medicine is a metabolic approach. How do you starve cancer? How do you starve bacteria and not hit them with a blowtorch like antibiotics, surgery, chemotherapy?

Emily is taking a metabolic approach to managing bacteria and microbial biofilms. I think the easiest word is mucus. If you ever don't understand that, there's one thing I would say is

Avatar the movie, and how they're all connected to the earth, and if anyone remembers that movie, there's connection; it applies to everything. I think everything stems from bacteria. Financial markets which I love, everything [about its behavior] you can learn in a lab, and you need an empathic approach and that is what one of the things we look for and what Emily has, is an empathic approach. I would call it almost playing chess. I actually think every company should have a master chess player who can work 15 moves ahead and all the "what ifs," game theory so to speak.

With that, we invested in Cohero and Primal on the same day and I made sure that the money cleared for Primal first, so that we could always say it was our first investment. Not taking anything away from Melissa or anything, but maybe I'm crazy, I'm passionate about everyone here but I think you guys are about to hear and it may not all be clear today, but you're about to hear about I think the most interesting company (technology) I've come across in 10/20 years and certainly the first one I've come across where I've been able to invest. [Emily,] I set you up.

# Primal Therapies, Inc

[P5HV - November 2016 - Presentation - Primal Therapies.pdf](#)

## Emily Stein:

I did my PHD in microbiology at Berkeley and I studied how microbes in the soil respond to stress. When they get stressed, they respond and they communicate with each other. They do these really cool things. They work together to defy that stressor. I tinkered with bugs for six years of my life. Then, I went across the water to Stanford. I worked in rheumatology. I played with people's bones and their immune cells. I studied rheumatoid arthritis, lupus and MS. There's a huge link between the organisms that reside on you and in you and how your body reacts with them. That constant communication literally happens every minute of every day of your entire life.

The seats your sitting on contain biofilms. Your cell phone contains the most disgusting biofilm; you probably don't even know. It's gross. It freaks me out. The hotel room I'm staying at, the remote control that I have a bag around right now because I don't want to touch it, contains biofilm. It's everywhere. Every culture, you name it. It's on the food you eat, it's everywhere. If I was more of a hypochondriac, I'd be a germaphobe.

[Slide 2] This is my grandma. Grandma Thelma. She's been my best friend for about 20 years. She's had rheumatoid arthritis for about 35 years. Her joints have fused. She can't bend her knuckles anymore. It really compromises what she can do. Eating is difficult. Writing her name on a check is difficult. What happened about ten years ago, she didn't tell us about, brushing her teeth became very, very difficult. She lost the battle to those guys. This is a picture. I could basically stain any of our mouths and it would turn out like this. That is the ... The blue is actually the biofilm that lives in your mouth. It lives and it hangs out at the interface between your teeth and your gums.

When you start to lose the battle, what happens is that they over grow. They take the food you eat, convert it to waste products which really upsets the balance in your mouth and can cause tooth decay, periodontal disease. What happened to my grandma was tooth loss. It was really sad because she stopped smiling. She stopped talking to her neighbors because she was embarrassed. The social impact was really ... It broke my heart. As a scientist, I started freaking out. This is what was really happening. The bugs were gaining access through her gums into her circulatory system and then, setting up shop in her joints, brain, heart and lung.

What happens ... We're finding out, if you have periodontal disease ... Believe me, one out of two people in this room, likely have periodontal disease. It can cause other things. They're now linking it to pancreatic cancer, esophageal and lung cancers. They're linking it to atherosclerosis. They're linking it to dementia. Scary stuff.

About the same time that grandma started losing teeth, she started having strokes. Stroke is a significant risk factor to periodontal disease.

[Slide 3] I had to do something. How do we help grandma? It turns out that the mouth is a really complicated thing. There's a lot of things going in, all the time. Every time you eat or drink, you're influencing that system. There's also a host factors, right? Your tooth structure. Whether you drink bottled water or tap water, which has fluoride. It's also impacted by what you eat. How much sugar you're eating everyday directly influences these guys, who are living on you. It selects the good guys or bad guys, depending upon what you're eating. It definitely effects how abundant they are in your mouth.

What we're doing is, we took a unique approach, probably because I'm a microbiologist. I focus on the bugs. Not my grandma's diet, I focused on her bug's diet. The fastest impact I can have is if I interrupt what her bugs are eating to create direct change. What we did is we took a very logical inexpensive approach. We took FDA approved ingredients, that are recognized for being safe, have been used in foods, have been used in vitamins for decades and we screened them on real biofilms from people's mouths and pathogens that are known to colonize the mouth. And basically asked the question, "Which ingredients stop the bugs from using sugar?" That they no longer make acid ... Which is inflammatory. They no longer make plaque.

Turned out they were super low cost. Not only that but, a lot of them are compatible with traditional formats like chewing gum or mouth wash. What we came up with was a little mint. We put the ingredients in this mint that my grandma can take multiple times a day because she can't brush her teeth. In her care facility, they only brush her teeth once a day ... Which no one really talks about. That's not good.

At least we can protect her mouth. She takes this. Sucks on it. Releases the active ingredients, coats the surface of her mouth, binds to the surface of the bugs in her mouth, blocks the ability of the bugs from using the sugar that she just ate and stopping them from making plaque and acid.

We asked, "Well, does this work for other people besides my grandma?" We did a 25-person study ... Perfect concept study. We measured their PH before [Slide 4]. If you remember back to chemistry or high school science class, PH is a log scale. Seven is neutral. Your blood PH is about 7.2. PH of six is acidic. Your tooth decay starts at a PH about 6.2. These people, after taking a single tablet ... We followed them for about 60 minutes afterwards, you can see their PH is all in the neutral range. We completely changed their mouth environment from a disease causing environment to more of a health promoting environment.

We also asked what the effects of these ingredients might be on pathogens in the mouth. We look at strep. Strep causes cavities. We looked at three bugs, which I'm not going to name for you because you won't know them anyways. They're hard to pronounce. They cause periodontal disease. We asked, "Okay, 22 people. Kids and parents, if they take it 3 times a day for 5 days, what affect does it have on the bad bugs in your mouth and what affect does it have on the good bugs in your mouth?"

You can see, there's a definite drop or change from base line to five days after [Slide 5]. We're reducing the burden in the biofilms of the bad guys that are causing problems. We're maintaining the levels of the good guys. You need those protective bugs in your mouth to take care of you. That's what the data is showing.

[Slide 6] That leads us to a lot of opportunities in the market place. Where could these ingredients go? It turns out that the oral care market is pretty antiquated. For instance, one of the largest ... Biggest brands to mouth wash was first a floor stripper. People are swishing their mouths with a floor stripper that causes oral cancer.

It's a large market, lot of players. Procter and Gamble, Johnson and Johnson, GSK, they all have their big brands. The best way to get our ingredients in the market is, put it in their products [Slide 7]. They have the sales channels and we don't have to build that infrastructure. We do have to message to them. We do have to have compelling data. That's one of the things we're in the process of doing with this funding is, setting up and building these amazing efficacy studies to get the data they're going to need.

Basically, the goal is to get them to de-adopt all these hazardous ingredients that kill the bugs and hurt your own cells and to replace them with our healthy ingredients that were built in a more derived and intentional way. It allows them to position themselves better in the market place. To maintain their share or even grow their market share.

For instance, if we did a deal with any of the players on this, passive revenue from a non-inclusive license is about three percent annually licensing fee. That would equate to about four million dollars annually of passive revenue per toothpaste, on one of the lower guys. These guys, it's much more significant. The goal is to get our ingredients into multiple player's hands.

We're already in conversations with companies ... They want to coat their dental floss with our ingredients. A couple companies want to white label the mints. Basically, just for oral care, there's a significant market for this formula.

[Slide 8] Enough about humans. I'm a huge animal lover. This is Tinsley. I flew all the way up to Washington State to rescue her. She was at a shelter. I talked to the vet and she wasn't doing well at all. She had massive infections. It was from her mouth, turned out. I flew up there, rented a car, drove her all the way down to the bay area. Windows had to be down the whole time because she had this atrocious breath. Got her on a Saturday. Got back. Emergency vet appointment on Monday. 26 tooth extractions and \$4,800 later, this is Tins. She's super healthy. She can't keep her tongue in her mouth anymore because she doesn't have teeth but, she's doing well. She's not alone.

Eight out of ten ... 80 percent of dogs over the age of three have problems. I spend a little more but most people spend about 38 percent of their expenditure annually on oral care products for their dog. The cool part that I went after and I exploited is the fact that it's known that owners and their dogs share the same bacteria in their mouth. It's kind of gross when you think about it but, it's true.

We asked, "Okay well, does the first formula work on dogs?" The answer is yes. The problem is dogs ... You're not going to have a dog and treat a dog after they eat every time. We created a second formula which is even stronger so you only need to give it to them once a day. That's in development and we're setting up to do efficacy studies.

While I was building it, I had a really great friend who came to me. She has a King Charles and he had knee replacement surgeries at UC Davis [Slide 9]. After surgery, he acquired multi drug resistant infection in his skin. He'd been colonized by some really bad bugs when he went to the hospital. Long story short, wound up getting massive skin infections that would spread up to a quarter of the size of his body. It was untreatable. This is him ... His name's Rocky. This is Rocky on antibiotics with oral and ointment. You can see it's really angry looking and inflamed. It was refractory to treatment. She asked if the canine oral product would work on her dogs skin. I'm like, "Let's see." She applied it every day for ten days. You can see ten days later how his skin looked.

Recently, he's had another outbreak on his stomach. This time, she did not even apply antibiotics. You can see how it stopped lesion progression after one and half days. We're really excited about this. It's obviously a platform [Slide 10]. We can explore additional ways to use this formula and the other formula to address unmet needs. Really what we're dealing with is the way we think about biofilms and the way we like to tinker and to influence them, to get them to do things that promote health. These are just some of the things that we're really gearing up to investigate and try to derive value.

[Slide 11] I want to thank you. This is grandma. She's doing great now. She hasn't had a stroke in like a year. She's doing awesome.

**David L. Eigen:**

I'll just quickly mention that Suzanne Szabo is here who's joined Emily. She recently was head of microbial research at Novartis, and is completely moving in the direction of working with someone because it's such a novel approach.

The next company is another who we think has potentially ground breaking technology. It's not necessarily something that doesn't exist, but it's wildly expensive and used in big labs like at Novartis. Biorealize is bringing synthetic biology basically down to a cost that you could have at every school. You could have it at home, like a 3D printer or a PC of yesterday. With that I will turn it over to Orkan.

# Biorealize

[P5HV - November 2016 Presentation - Biorealize.pdf](#)

## Orkan Telhan / Biorealize:

Thank you David, Aaron, Dan and Charlotte for inviting us to this amazing event with very likeminded people. We are very happy to be here because it's probably rare that you will see a designer and a biologist, Karen and I, in the same room talking about the future of biology, synthetic biology, biology for design, microbiome work through the lens of technology which is I think, we think it's going to change the future of research in synthetic biology and microbiome work once and for all. What we are going to tell you is a story about how biotechnology has been researched, has been applied, has been developed in the past for the past 50 years, and how is it going to be researched and developed in the next 10, 20, 30 years, because there's a big massive change right now in the way we work with biology.

Right now 75% of every product that is produced in the United States is using biochemical processes [Slide 2]. Big pharmaceutical companies, from agriculture to material science, from DuPont to others they are using biotechnologies. It's a big growing market, but we want more people to get involved with it. One way to do is, is to really bring that technology into the hands of people who don't have that opportunity yet [Slide 3].

Outside the US, obviously have other places that have different kinds of problems, so we are not only interested in making new products, new people to design new products using biotechnologies, but also people dealing with very fundamental issues related to the environment, climate change, health care, diagnostics, in places where technologies and infrastructure doesn't exist.

We want to also think about outside, the rest of the world, where a lot of people can use these technologies to deal with their own problems in their own capacities. We want to empower them so that we can really change the planet also for the good. How do we do this? [Slide 4] Today a lot of people work at biotechnologies in lab settings. We have heard many amazing scientists today who go to very prestigious institutions, they get top-notch education, they work in million dollar labs, and they work with infrastructure that has been given to them, but they still most of the time use manual labor, after many years of training, and they still follow a very traditional format. I would say if you imagined the early days of punch cards and computation, they are still working with punch cards in the world of biology and medicine, so we are interested in changing that.

How do we do this? The word that came up quite a bit today is the microbes, that we work with microbes, and how do we work with microbes? How do we design microbes so that they can turn into mini factories, so that they can grow things from insulin, to new materials, to food supply, to probiotics, to food supplements, all sorts of different things so that we can really term them the new way of manufacturing or fabrication? We have built a platform that basically alternates the process of inserting new kinds of DNA inside bacteria [Slide 5], so that you can turn the bacteria, grow the bacteria with certain capabilities, so that they can design new products for you. You basically alternate the whole process so that you don't really have to know a lot of biology to be able to develop new products.

Scientists like Emily or designers in different parts of the world, can collectively collaboratively work together to really design new products without necessarily knowing too much biology. How do we do this? Let me show you a small video that explains, and I will explain the whole process. This is our first prototype that we have built two years ago. Basically using, doing biology should be as simple as adding bacteria and DNA on one end, let the machine take care of the rest, put the DNA inside the bacteria so that the bacteria can actually grow insulin, grow biomaterials, or actually grow new kinds of proteins that can be applied in all sorts of healthcare and pharmaceutical products. Now take the bacteria, grow them with different kind of nutrients, test their resistance to antibiotics, yes you can use this platform to design new kinds of antibiotics and research antibiotics.

Then at the end when your tests are done, take away the product, then directly apply in wherever you want to use them. For example, you can grow concrete that can actually heal by adding self-healing bacteria inside them so that they can actually make furniture, make buildings that can repair themselves over time. It's not only about really augmenting these products for healthcare and pharmaceutical technologies, but actually giving it to the hands of designers, who can be fashion designers, product designers, architects, all sorts of people who can now design and work with living organisms. From the idea to the invention obviously there has to be a business [Slide 7]. If you're interested in turning this into a business, because there is right now very limited access to these kind of technologies because it's not so easy for you to get organisms.

If you're not in an academic institution or working in a big company, you won't be able to order DNA or get organisms in your hand, so we want to provide the ways to distribute these organisms in a safe and sound way to the right people, and then actually have these people work with a standardized platform so they can work together with each other, in a networked way, so that they can benefit from each other's products and each other's researches. They can collaborate. They can validate each other's research, which is a fundamental problem in the sciences. Everyone can invent a new ... Come up with a new scientific discovery, but repeating and verifying that research is often difficult. We need a standardized platform, so we provide that.

Ultimately give everyone an ability to produce the products, and at the end pick up their waste so that they don't have to litter them to the environment and cause some pollution. We're interested in giving these resources, and rather than design the products, grow the products, and then eventually remove the waste so they can only focus on the design. A little bit about what is out there so that you can ask yourself, Orkan, what is really right now people are doing, so what are you really transforming? There's a couple of trends in the industry right now. There's very expensive equipment [Slide 8].

If you're lucky enough to get these very big million dollar grants from NIH or NSF, you can invest a lot of money in robotic equipment that is there to fill a big giant room, and which can cost anywhere from 250,000 to a million dollars which will allow you to do this kind of research, but we want to aim to a priced one where it gets so cheap that everyone can actually buy, maybe a dozen of these machines and link them together to do more collective research. Another trend, maybe you already heard about this is cloud site biology. You don't have to own an equipment. You send them somewhere in the cloud, your experiments you want to run,

many experiments but then you send them to the cloud. One company somewhere else does it for you and send you the data, but this is also an approach that we are posing.

We want everyone like a PC, or like a personal computer own a device, whether it's a school, whether it's a design office. Whoever can afford a 3D printer or a laser cutter, have a device like this and get their hands on so that they can start inventing new products. I think that will become the most important part of the technology. As David was alluding, what kind of a company we are, what kind of a future are we imaging for ourselves. We imagine ourselves to be not only to be a platform company, but also a network company as much as Google, Amazon, and Uber is [Slide 9]. We're not interested in designing machines that will enable consumers at the end. We want to enable producers.

We want to deliver, we want to traffic new kinds of consumables, new kinds of products so that whoever has a machine that is connected to a network becomes an inventor in a way there so that we can start enabling them for new kinds of product development. This is our team [Slide 10]. Karen is our biologist. She's going to speak a lot about how we can actually utilize these in a concrete set up. Mike is our engineer and we have a business advisor already on board. We are getting together to launch ourselves into more advanced, more investment and more funding so that we can really hit the road with manufacturing a lot of machines. I will pass it to Karen so that she can describe what a biologist would do with a technology like that.

#### **Karen Hogan / Biorealize**

Hi, I'm Karen. Thank you for having me today. It's a real joy to be here and learn about all of these companies. As Orkan said, I'm a biologist, but one thing I do on a daily basis is educate a lot of undergraduates about biology and now about design as well. I never imagined that I would enter the world of design. I do like creative ventures, so I can't say that I'm all that surprised that I find myself here. My real interest is in Microbiology and applying the knowledge that we gain to real world products. When Orkan turned me onto the idea of biological design, my first question was what is that? I don't really understand how you would design with living organisms [Slide 11]. Then he showed me a lot of different examples that are up here as products.

For example, the self-healing concrete, the idea that when concrete gets wet, it cracks. Well, if you put certain bacteria in there, actually when water gets into it, it can form silicone and heal those cracks. This is all part of the movement of biological design. Different materials that will react to your sweat for example and cool you instead of you having to air condition a large room like this. This is the future of design and of the products that we're going to be producing. When we bring students and designers into our lab and show case this technology, the first thing they say is, "Well that's fabulous, you have this beautiful looking machine that is spinning and is really exciting, but what can I do with it?"

We thought we need to give people a really good example of how to use the machine that every person in this room could do. It's near dinner, you're probably hungry, and you may enjoy donuts. [Slide 12] We decided, "what if we teach biological design through the lens of food design?" Here we have microbial donuts. They're beautiful. It think you hopefully will like the form factor, but the way we can bring designers into this conversation about biological design is really to think about the aesthetics of the donuts, thinking of different form factors for the donuts, and so we cast these beautiful molds that look like diatoms which are really nice

creatures that live in the water column and instead of baking your donut with regular baker's yeast, we actually take yeast that's been transformed or modified to make beta-Carotene.

It will be a lot nicer to get your beta-Carotene through donut than through a carrot, or at least my kids would agree. One of the things when you start doing this design, is that these living organisms are finicky. I'm sure Emily and other people who've spoken today will agree with that kind of domesticating and taming these organisms is a problem, and so it takes a lot of prototyping to do that. What you see up here [Slide 13] is some yeast that are making beta-Carotene but unfortunately some of them have escaped our control and are no longer making that compound. A big part of the design process [Slide 14] is actually going through that prototyping and doing it in an efficient way.

As a grad student I was the efficient way. I worked extra-long hours at the bench, pipetting things, moving liquids around, and that prevented me from kind of using my brain power to solve other problems. We decided that that's pretty antiquated method and if you can free people, liberate them from tests that a robot can do tirelessly, repetitively around the clock, then you can release them to think about things like microbial donuts. Here [Slide 15, Slide 16] we have our designer working on baking with the donuts using icings that now might contain probiotics in them. The donut itself would deliver the beta-Carotene but the icing might contain some drug for ... Might contain something like insulin for example.

We teach our students and we train designers on how to use this machine, by bringing them into these workshops [Slide 17], and so you can actually see this beta-Carotene producing yeast growing in our syringes [Slide 18] and going right into a recipe. Here it is up close [Slide 19] , and we do this all using this single platform of a plug and play. You design something conceptually; you order the consumables; they arrive... you put them into the machine you; press go, and out the other end comes this wonderful yeast. This doesn't have to be something just like a bio-fortified donut. You can imagine that you could deliver many products this way and when you think about the end user in product design, then you really can create some very powerful changes. No more shots, no more small pills that when they fall on the floor you can't see them, no more things that taste bad.

Instead you could really reimagine this entire industry disrupting a lot of how drugs are delivered so that you're really designing things for the end user. That's our hope with technologies like this.

## Closing remarks

### David L. Eigen:

These are all things anyone who would like the presentation we can talk about [print or email to you. But note it is coupled to this transcript]. These are all things we hit on before, what we do and how we think we do it differently. The one thing I would say is that, as, I mentioned earlier, we have what we would call an ecosystem... Everything comes back to complex biological systems... The understanding of that and what we're trying to do and adding, every time we add someone great, whether it's a businessman who could advise our company or another scientist. We're making what we're doing collectively better.

I remember back in college and this professor was in Middle East political science. He said, "There's a belief in the Middle East, you're either moving backwards or forwards, there's nothing in between." That's what we're doing. We're moving forward and our goal is to help people. We're not in this just to make money. There're a lot of people out there. We've met a lot of venture capitalists over the years. They're strictly out there to make a lot of money. You see MBAs going into this, you see all these undergrads, all they want to do is be a venture capitalist and forever, venture capital was a retirement place for people who worked [in companies or typically founded them]. Traditionally in Silicon Valley, they were 40, 45, and they had been through everything. I've been through a lot and this is where I want to be; this is where Aaron wants to be.

He got sick of things being caught in academia and here we are pushing forward. Another thing I'm not even going to get into reading except at the very bottom. [Slide 19 - Terms] What we're doing with the fund, anyone that's interested we can talk about it. We're doing a closing right before Thanksgiving [now [January 6<sup>th</sup>, 2017](#)], and we're going to do another closing in January [Now February]. With that, I want to thank Charlotte who is right there. Probably saw her face on the bottom right corner during Melissa's presentation. She runs P5; she's run my life for over four years. She does everything and she pulled all of this together. I have to thank you and with that I'd like to go over to cocktails. In the back though, which Cindy (David's wife) is about to put her hand out like on Price is Right.

Our book, I cannot tell you how great this book is. It is called "I Contain Multitudes." Dan knows the author; he's going have him at Penn soon so anyone who wants to fly up in the dead of winter, you are welcome to. That book, there are copies for everyone. And then there is Emily's first product [in the form of mints for human use], and there's a handful of [oral] dog formula [bottles] which I actually used on my mother's dog in the last two days and she has sores on her belly [as her belly rapidly cleared up despite an otherwise recurring problem, it seems to work in all places there is strep and or staph]. Unless I'm crazy or just Hyper optimistic, I'm seeing a dramatic difference. Oh and she saved me from I don't know what other throat ailment; so this stuff works, so thank you and I look forward to talking.

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