Rare Disease, Big Impact

Speaker: Matt Wilsey, Founder & CEO of Grace Science

Interviewer: Randall Ussery, CEO, Free Range

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Transcript:

Welcome to Babson San Francisco. I'm Lynn Santopietro, I'm the Director [at Babson San Francsico]. Tonight we're thrilled to kick off our third Thrive event. We have Matt Wilsey from Grace Science, who will be interviewed by Randall Ussery, who is the CEO of Free Range, and Babson alum and also teaches here at Babson as well. Thanks for being here and we look forward to a good discussion.

Randall Ussery: So I had the chance to meet Matt about 18 months ago I think. We were having a conversation down in Palo Alto around what he was up to, and it was probably one of the most inspiring conversations I've had in a really long time. I thought this would be a good forum for him to share his story and what he's up to. Maybe you can talk a little bit about why we were sitting there.

Matt Wilsey: So my background, I'm a tech entrepreneur, that's what I identify with the most. I've been in involved in three tech startups. I shifted gears pretty dramatically when my daughter, Grace was born. She's 7 1/2 years old now. We knew something was wrong in utero, and it was actually kind of a sort of awakening when the doctors ... at the time we were living in New York, and they outlined the options for terminating the pregnancy, and we just explained that that was not an option for us. We were going forward no matter what. Whatever cards we were dealt with, we were going to deal with it head on.

Grace was born. It was an emergency C-Section at Stanford University, and we knew

something was wrong right away. I think it sort of mom or dad intuition, but I can actually remember the moment where my life changed. I don't think many people are fortunate or unfortunate to know when that moment actually is, but I actually can remember it vividly. I just thought there's something wrong with Grace.
So that set us on the path that we are today, and where we're going.

Randall Ussery: So Grace was in NICU for just a number of days and the doctors kind of handed you a decision, in respects.

Matt Wilsey: Yeah, exactly. So it was about two and a half weeks we were in the NICU, which is a harrowing experience by itself. For those fortunate to come out of the NICU, it's life changing by itself. For us the doctors essentially said there's nothing more we can do for you here. You should go home and monitor Grace as an outpatient. So we kind of felt like we'd gone to the edge of science and medicine with her in the first three weeks of life. And I was thinking to myself, 'there's nothing more you guys can do here? This is it? This is the extent of our knowledge'? So we felt like, OK - then we'll pick up the slack where they aren't able to continue.

Randall Ussery: When you arrived home, you kind of had a choice, and you were given really three choices. What were they?

Matt Wilsey: They didn't say it this clearly, but the three choices we really had were basically go home and enjoy your daughter for as many years as you might get. You could think about starting your own foundation, and kind of building the pieces of ... almost like a medical research institute, or you could potentially join something that' larger. Since we didn't know what Grace had, who were we going to join up with? I mean, do we join up with like the Michael J. Fox Foundation? Do we join up with Deuchenne’s Muscular Dystrophy. The sky's the limit. And if you're off by an inch at launch, you're going to be off by miles in obit. So it was like, I think we need to take control of our own destiny and start our own foundation.

Randall Ussery: So you set off on uncovering what she has.

Matt Wilsey: Many people don't know but there's 7,000 rare diseases that exist today. That numbers going to increase quite dramatically with the advent of Whole Genome Sequencing. A rare disease is classified, at least in the United States, as something that affects less than 200,000 individuals. If you think about it, 200,000 individuals is a lot of people. It's pretty amazing that that's how it's classified as a rare disease. In Grace's case, we now know that there's less than 50 people in the world confirmed with what she has. Just to kind of put it in perspective, less than 50 in the entire world. So this is ultra ultra rare.

It goes back to being an entrepreneur, but especially a tech entrepreneur, where in my mind, I wanted the data. I want all the data that I can get my hands on. I would think most entrepreneurs would think the same thing, even if they're not in technology. I'm not sure how I'm going to analyze it, I'm not sure what I'm going to do with it, but lets get it in our hands and start working with it. So that's what we did. We did a whole genome sequencing at two centers, two of the top centers in the United States. At Stanford and Baylor College of Medicine in Houston.

They both came up with the same root cause. It happened to be the wrong root cause. This is what happens when you're pushing the envelope early in any field or discipline that you guys are going to go into. But we said let's keep going, let's keep pushing. And just like the Google algorithm, it gets better the more you search. Either personally or also the community. So we went back to the teams and said would you please re-sequence Grace. And they did. Keep in mind, at this time, no one was doing whole genome sequencing. This was really cutting edge stuff.

Randall Ussery: How many years ago?

Matt Wilsey: About 5 years ago we started. Six years ago. Some people were doing whole exome, which is just a small portion of our genetic code. We went back and they were able to actually pin point what the root cause was with repetition. The analogy I use with many people that aren't scientists is imagine if there's a blue wall and you want to paint it white. Well if you just do one coat, you're still seeing the blue through the paint. So you have to keep going over it repeatedly. That's what we did until we were able to find the root cause.

Randall Ussery: So you uncover the root cause, and it happens to be NGLY1.

Matt Wilsey: Yeah.

Randall Ussery: What is that, in laymen's terms?

Matt Wilsey: NGLY1 happens to be a gene that all of you carry, and all of you have at least one healthy copy of this gene. Of all the genes in our body, there's 20,000, we typically inherit one from our mother, one from our father. There's a few exceptions to that of course. In Grace's case, she inherited two bad copies. One bad one from me and one bad one from my wife Kristen. It was just a random thing of bad luck that really couldn't have been prevented because the disease had not been identified at that point.

Randall Ussery: So when we met, you were about three years into this process of uncovering NGLY1, and then understanding how to actually think about gathering as much data as possible. You were also dealing with the side of the government as well as just the industry itself of how are you going to solve for a rare disease, right? You didn't just want to improve the quality of care, you wanted to think about curing, right?

Matt Wilsey: Yeah. That was kind of in our original three options. Improve quality of life somehow, but I wasn't going to just stand at improve quality of life, I really wanted a cure. If you say that to people in science or medicine, they dismiss you almost immediately. There's not many cures out there. There's less than 10 probably, real cures, technical cures. There's a lot of treatments for high blood pressure or diabetes, but they're not cures. I said, well, I want to cure this disease, and in the process, we're probably going to find other things that we could potentially treat or also cure.

That has been our mantra since the get go. And part of that is finding the best talent that also believes in that vision. From my days and an entrepreneur, John Doer was involved in my first tech startup, and he said it's really important – and actually probably would be more closely attached to someone like Bill Campbell or Randy

Komisar – but they said it's really important to hire missionaries, not mercenaries. It's easy in science and medicine to hire mercenaries. People that are just going after grant money, but are not really interested in the patients. Would they be pursuing this if they weren't being paid to do it?

[00:10:00] That's where the hard part comes in, is finding people that believe in the mission and they're going to be working 24 hours a day to make it successful.

Randall Ussery: Yeah, maybe we can go into a little bit ... it's a terminal illness, right?

Matt Wilsey: Yeah.

Randall Ussery: She has 12 [years] potentially, but we don't know.

Matt Wilsey: Yeah, the oldest patient that we've found is 23 years old, but she's slightly deteriorating. We lost one of our patients last May who was a 4-year-old. So we're not really sure where the end comes, but we're working like it's tomorrow basically.

Randall Ussery: And so when we were having our initial conversation, a lot of what we were talking about was, this wasn't a $2 million operating budget problem, right? That the size of the foundation at the time, this was a larger need for access to capital to go and explore what the opportunity could be to solve for this.

Matt Wilsey: Exactly. And the thought process behind that. It's interesting because we've probably been more successful than 99.9% of foundations out there in terms of fundraising. And as generous as our family and friends and just the general public have been, it's not enough to cure something like this. The great thing is that the way science and medicine is developing is that things are becoming cheaper. So my feeling is instead of costing $100 million to $200 million to develop a treatment, could we do it for $20 to 40 million dollars. Because if we could, there's a potential for both investors, but also the government to step up on things like that. It's a simple cost benefit analysis.

In our case, we felt that we could raise a lot more money as a for profit entity. We just had to be very concrete that it is a risky proposition, and it's going to take some time. But the return on investment is absolutely possible. And there's other companies that are also showing this now, which is exciting for us.

Randall Ussery: Yeah, and if you solve for one rare disease, you have the potential to solve for other rare diseases. I think there's a statistic 1 in 10 people on the street that you pass has a rare disease.

Matt Wilsey: That's right.

Randall Ussery: You just wouldn't know it. So if you look at it from an aggregated perspective, there's a lot bigger opportunity. You have the access to capital issue, or the need for capital to go and do something. But then you're also facing an industry that is kind of water falling in respects. Let's take your background from a tech perspective, and thinking about how you were agile and moving really fast, to where you're playing now.

Matt Wilsey: I think we still are very agile and fast, it's just not as fast as I'm used to.

Randall Ussery: Right.

Matt Wilsey: So the scientists are always like, I don't know if you realize this, but you guys are going at warp speed. But of course as an entrepreneur, you can always go warped plus 1, or what is the additive.

We can always improve. If you think you can't improve, you're pulling someone’s chain. There's always room to become more efficient. So that's what we've been trying to do.

I would say that the industry we're playing in does not like to change. Partly they're just risk adverse in general in the liability of that. And partly it's because they just don't want to disrupt their revenue centers. They have of course, Wall Street to respond to. As we say, look, our shareholders are our patients, and so we're not really setting the time table for the disease. The disease is setting the time table for us.
We're trying to work back from that. I would say initially – and I think to this day most of the CEO's that we talk to in pharmaceutical companies will say – there's just not

enough patients for us to be interested. And even if we could convince one of them to take us as a project, they won't be there probably in 5-10 years. So then what's the first program that gets cut? It's the one with the smallest number of patients. That's where again, it comes back to taking the bull by the horns and controlling your own future.

Randall Ussery: And then coming back to what Komisar said, around missionaries, hiring missionaries, and thinking about being a little bit more patient centered, I think you were kind of facing that as well, against the mercenary aspect of the industry at times. Not holistically, but you're wrestling with a daughter that's potentially going to pass because of this disease. How do you get people to understand that emotionally. So talk about the building of your team and how you brought them together.

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Matt Wilsey: Initially it was, who's the best at X, or what is our biggest gap in our platform right now? What could get us the fastest answers and the cleanest answers. We started to triangulate on a few different areas, and then from there, a few different candidates. We don't put out RFP's and say would the world please apply to this program. We're offering money. We felt like we would just be totally overwhelmed responding to those. Reading them and then responding. So we cherry picked the best of the best. So imagine if you're starting a new search engine you'd go steal from Facebook or Google or Twitter. You'd go grab those people, recruit them. So that's what we did. There were no subject matter experts on this disease. We wanted to build the team. Almost like a Manhattan Project. We wanted the best of the best. And then they started to recruit people for us. You guys have probably seen this in your careers, is A+ talent wants to be with A+ talent. And they start policing themselves in a way. They start, you know, you don't want to be on the next monthly call and not show that your work has been meaningful or successful. So you're going to work day and night to make sure that you're going to have something meaningful.

Randall Ussery: But even though you had an outcome driven mission, you were also lending them autonomy in collaboration that they hadn't had in the past, right? Maybe speak about that.

Matt Wilsey:	That's a great point. In a true startup sense, we don't want to micromanage the talent. If we've done our job bringing on the best people, you're works done. Now it's about creating the environment where they can be successful. We wanted a really flat organization with no heiarchy, and our only request was that they shared openly amongst each other.
Randall Ussery:	This is very uncommon.
Matt Wilsey:	It just does not happen.
Randall Ussery:	Maybe talk about the industry as a whole in that respect.
Matt Wilsey:	Yeah, and especially within academia, most scientists, most researchers, really want to hoard the information for themselves. And it's kind of Lord of the Flies in essence. It's sort of like, they have to publish papers in order to get tenure. And in order to publish, they need data that only they have access to, or that they can do meaningful things with. And it's not like – I'm sure people in industry or academia that watch this will call baloney, but it's very true. There are many silos where people aren't collaborating, aren't communicating. So we said you're going to have to do something different here because were at limited time and we don't have ... not only limited time, but limited patience. There's no margin for error here. We can't do like a 5 year double blind placebo study on these kids. Like where someone gets fruit juice and someone else actually gets the drug. People started to buy into that. There's been some people that have not bought into that model of openness and collaboration.
Randall Ussery:	Part of that's because of IP licensing rights.
Matt Wilsey:	Some of it, yeah. Securing futures. And some of it's just that they need to publish, and in order to publish, they need to protect their data. Those people aren't long for our team. Just to put it nicely. They just don't fit with the mantra of the team. In a way, I

feel like we created the spark, but now it's the teams philosophy and vision and it's evolving constantly. SO it's whatever works best for them. But always keeping, again, the patient as our number one decision point, which sometimes makes us unpopular.

Randall Ussery: And we're starting to see a shift in that philosophy at the government level, right? NIH and the FDA, being a little bit more patient centered, focused first.

Matt Wilsey: That's right.

Randall Ussery: Talk about that a little bit, because that's not always common as well.

Matt Wilsey: Some of this has been started past administrations. For all the worry and short comings with President Trump, one of the things that was actually encouraging at his joint address to Congress is that he did talk about rare diseases and one patient in particular that suffers from Pompeii disease, which is pretty remarkable to have a President actually address it to Congress.

There is really bipartisan support for it, and I always say this to people. The FDA's not the problem. The problem is that we're not putting good enough compounds in the top of the funnel. If we increase the number of compounds going into the funnel, or therapies into the funnel that are much more efficient, they're going to get approved. My feeling is that the FDA's doing their job. There's probably ways that they could become more efficient, but we're not there yet. We'd be lucky to be there. We hope to be there soon. We still probably have some years left.

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Randall Ussery: Do you want to go into your business model, or your platform model? Just kind of explain that, what you are doing that may be a little bit different or it's replicating some best practice that's out there already that you've seen.

Matt Wilsey: For sure. The idea is there's a lot of these rare diseases that are below the surface. I almost think of it as the iceberg analogy. Right, 75% or whatever is below the waterline. The same thing is true with rare diseases. Industry is focusing on the very very top of the iceberg. All that you can see, it's only like the top 2% that they're actually investigating and trying to develop drugs for. Our philosophy is that if you actually grouped all these rare diseases below the surface together, and understand what their connections are, maybe 10 of those diseases could benefit from the exact same therapy. So maybe it's not 7,000 unique rare diseases, maybe we're actually only talking about maybe needing to develop drugs for 1,000 or 500. Imagine how much more that becomes efficient, but also what the revenue potential is for businesses that think that way.

So that's only one part of our model. The second part is really bridging those to more common indications. That's at a macro level. On a micro level, we really think of our model as being centered around the team.

Randall Ussery: And if you have a chance to go to Grace Science, you should check out the team. It's a number of Nobel Laureates or future Laureates. Just a great advisory network in general.

Matt Wilsey: The idea is to focus on the set of advisors. These are always constant. Our team, our advisors and then our network, which really goes to ... it all goes back to being an entrepreneur and the roots of being an entrepreneur, in that I think a lot of what we've applied all comes from my time and my three tech start ups. I say startups, I mean they're real companies now, you know with real revenue and the last one was acquired by Twitter. So it's a product that will live on for a long time.

The idea is to leverage these cores, the team, the network, and really traditional business development principals. Then think about diseases that are rotating around that core and how they link together. I almost think of it as a cryptic's lock. There's some combination that we're just not sure of yet that's going to take time to tease out, but the combination's there.

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Randall Ussery: And high level communication will actually be able to unlock that.

Matt Wilsey: I think so.

Randall Ussery: Opportunity, right?

Matt Wilsey: Yeah.

Randall Ussery: So let's move to the personal a little bit. We kind of started there, let's kind of shift back. What's it been like for you, gong through this process? And you have an MBA, right? You have a tech background also you studied in Politics a little bit, and now you're coming into an entirely new industry for you. How are you perceived, how do you perceive yourself? How do you deal with it on a day to day basis.

Matt Wilsey: How's it been? It has been incredibly hard. I would definitely not wish this on anybody. It's human nature that there's the fight or flee instinct. And I know plenty of people in our position that have stayed to fight, and I know an equal number that have fled the battle. And I respect both of them. And there's not a day that doesn't go by that I'm not like maybe it's time to throw in the towel. It is that level of stress and hardship. But it's one of those things that you just can't, or at least I can't. As I see Grace when I put her to bed, I literally can't give up, for better or worse.

There's been a lot of good things that have come from it. I say all the time that we've met literally the best scientists in the world, which is really cool. Like I sometimes have to pinch myself and be like I'm grabbing beers with this guy that won a Nobel Prize. It's amazing. And they would do anything for Grace. And I think that goes probably again back to the core of ... sort of the principals of being an entrepreneur.

Randall Ussery: I think it's good for everyone to know when I first met Matt, my child was actually in NICU, had been in NICU for some time and we weren't sure exactly what he was suffering from. I think we were 6 weeks in at the time when I met you. And Matt just stopped the conversation. It wasn't about him at all, it was just like, “How can I help you, this is what you need to think about, this is who you should talk to. Push back.” You kind of gave me the checklist, everything you had gone through. And was consistently checking in with me. This is someone on the other side that had been going through this for sometime, and it just says a lot about your personality, and also Kristen's. You just care, you care fundamentally, not just for Grace, but for the entire rare disease population.

Matt Wilsey: That kind of also ... we don't shy away from conflict, I think. That also creates friction within the ecosystem where when people say, well this is how it's done, or this is the way we do things. For us, if the way we do things, or the way traditionally it occurs, if it's slowing up a therapy for our community, or for rare diseases broadly we're going to address it. That could be uncomfortable. But that's also what I think it means to be a leader. It's like, Look, it's not a popularity contest. Difficult decisions have to be made, and uncomfortable conversations have to happen.

We hit those things head on. And Kristin and I are a great team together. I forget what the percentage is, it's like 49% of marriages end in divorce. In the rare disease world, it's like 89%. It's that much more stress on a relationship and a marriage, but this September we'll be married 10 years, and going stronger than ever.

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Randall Ussery: I've always loved how Matt ... I've had conversations with you late at night, around 8:30, 9:00, I don't know 10:00 and you're like, “I'm tired.” And then the next morning he's calling you, “I'm great.”

Matt Wilsey: The benefits of the espresso machine.

Randall Ussery: You started this foundation about 5 years ago. You've gotten it off the ground. You were able to assemble a pretty strong team. And now, literally right now, we're moving towards a for profit model. How do you think it shifts how you think about your day to day, and what do you think the future looks like from a business perspective in the next 2-3 years?

Matt Wilsey: Broadly, on the business side, or just our business in particular?

Randall Ussery: Your business in particular.

Matt Wilsey: The next iteration is starting a for profit entity. It's really a rare disease platform and the first target is going to be NGLY1 because we know the most about it. But the idea is taking NGLY1 and connecting it with bigger diseases that affect all of us in this room or online in some shape or form. Either our family members, or best friend, or cousin.

In the next two to three years, I set the goal of we want a therapy within five years. Grace is 7, so by the time she's 12, I expect a therapy, maybe even a cure, if we're lucky. But we might have to stop somewhere first and use a weigh station, and then keep moving forward. Buy more time.

I think in the next two years, hopefully in the next several weeks, we'll have closed financing. In the next two years, we'll have compounds that are in trial, of not approved. We set an ambitious goal. And then hopefully it will bridge into more common indications, probably in the next 5 years.

Randall Ussery: In the larger landscape perspective, it's been kind of interesting with certain conversations. Some people are saying it's a $50 million dollar problem, it's a $100 million dollar problem. Some people are saying start with $2 million. Where do you ... from a fundraising perspective, what are you settling in on and why?

Matt Wilsey: We're settling in around $7 million dollars as a seed financing. I would love $50 million. I'd love $25 million. I'd love as much money as investors would give us. The fact is, it changes the dynamics of the foundation, but also of the company. They both would be impacted by this. All of my tech start ups have all been very lean operations. Of course very challenging, but also incredibly fun. But it just allows us to operate much more efficiently. And we're not wasting money. And that's really important ultimately for our investors.

There's a lot of capital out there right now looking for good homes. The number one thing people say: “Don't lose my money.”

Randall Ussery: That's fair.

Matt Wilsey: Yeah, “Just don't lose my money. If I could just get my money back, I'd believe in what you're doing.” And that's very true. It's like investors aren't looking for private equity returns, especially in something like this where they believe in the social mission on top of the potential to make money, which has to be there. That's ... I've always scratched my head, especially recently, I'm like, capitalism is not bad. Capitalism is very, very good. And capitalism is ultimately going to lead to a treatment or a cure for my daughter. So we're all for that.

For us, it's just the next iteration. The foundation will stay in existence. It will focus on just NGLY1, but the company will be bridging into other rare diseases and the common implications like neuro degeneration and cancer. A lot of people say to us,” Oh my god, you're taking on cancer and neuro degeneration?” It's like, yeah, we are. Why not? Well, that's not how it's been done before. Well I don't care how it's been done before. This is how we're going to do it.

Randall Ussery: Right, and you have the backing of professionals that have been doing it for a very long time.

Matt Wilsey: Exactly, yeah.

Randall Ussery: We'll kind of end here a little bit before we go into the Q&A, but just a last question. Looking back 5 years, what would you have done differently? What do you think you would be doing now if you would have done it differently? It's a bogus question.

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Matt Wilsey: It is hard, because ultimately we have been successful. I always say, in a way we're like the tip of the sphere, right? So we're making a lot of mistakes because we don't have a lot of comparisons. There are a few, John Crowley or Brad Margus or Monica Conrad. I mean these are all people that have come before us. I think we've modified it more with sort of an entrepreneurial spin and especially a tech entrepreneurial spin. I guess ... I don't know if I would change anything. I really wouldn't. Maybe there could have been a few academic researchers that we could have gotten on our side a little bit earlier. There are people that do actively work against us, so I guess the challenge for anybody that's thinking about starting something, is how do you get those people on your side. In some cases you can't. It's impossible.

Randall Ussery: Yeah, how do you let them go?

Matt Wilsey: And how do you let them go? How do you ignore them. Which is even harder than anything. Because you want people to like you, right? You want people to be supportive of your mission. But no matter what you do in certain cases, it might be impossible. So it's one of those things where it's just like, we're going to go in two separate directions. I really respect you, and we're moving on. But it's hard for me to put on the blinders, so I guess that would probably be my answer. Learning to kind of let the water roll off the ducks back, in a way. Just kind of move forward.

Randall Ussery: Yeah, that's great. So I'll just kind of open up the floor a little bit to Q&A.

Audience #1: I just want to ask what is the disease?

Randall Ussery: What's the disease? Can you talk about that?

Matt Wilsey: Yeah, sorry, I talked about the gene ...

Randall Ussery: I was waiting the whole speech to ...

Matt Wilsey: Sorry about that ...

Randall Ussery: Why did they die and maybe go into that.

Matt Wilsey: NGLY1 is this critical gene that we all carry. It's involved in protein turnover and degradation. So proteins are being made in our body all the time to do various functions. They typically will have a sugar attached to them. And that shape, that form helps them do their function and then NGLY1's responsibility is actually to come in in kind of cut those sugars off. So then the protein can go to the protostome and be degraded. In the case of NGLY1 patients, because that sugar is not getting cleaved off, certain proteins, it really leads to cell stress and ultimately death. The patients are typically dying of infections, actually. So they get pneumonia, something like that, and they can't beat it off. Antibiotics don't help and they pass away from that.

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Audience #2: So far we've seen most of disease treatment post-natal. And with the advent of whole genome sequencing, do you see a possibility in the near to soon future of prenatal disease and rare disease treatment?

Matt Wilsey: Yeah, absolutely. For sure. I'm a big advocate of it. Some of these numbers vary. At one of the major sequencing centers that we're close with, of the undiagnosed cases that come in, they're able to identify now 50% of them, and out of that 50% it's amazing by the way, because before it used to take 7 years, and actually there's many patients out there that are still undiagnosed, which is really as shame because it does give some closure to know what you're fighting. But out of the 50% that are diagnosed, another 50%, so 25% of the total are totally random. So they're not inherited from mom and dad or the combination of the two. People will just say, you can just do IVF and just do pre genetic testing. Well, that's great, but what happens if it's a random mutation that happens in utero?

For the people like us where aborting is not an option, what do you do then? We're going to have to fix these babies in utero. So I would think yes, my hope is that with in, you know everyone gives like, oh yeah, within the next 20 years. I think it's going to happen much faster than that. I would start expecting some of this to start happening in the next 5-10 years. I hope it does. And I hope the major children's hospitals start sequencing every baby that's born. Offering that as something that they give to the families. As in families can opt out, but I think it'd be really valuable to then go through your life saying this is my genetic information, and I'd like to understand what my risk is for Parkinson's or breast cancer or whatever it might be.

Audience #3: There are a lot of different commercial genetic testing that is happening I think, like 23 and Me and things like that, are you able to partner with those companies in any way? And how do you see that growing in the future as all of us enter our genetic information into this research?

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Matt Wilsey: We do have a lot of conversations with companies like 23 and Me, Council, the big sequencing centers, academic centers. What we've been looking to them to tell us, specifically just on NGLY1, is do you see any patients, or healthy individuals ... there's something called resiliency, right, so let's say someone like myself has two NGLY1 mutations, but does not present like Grace does, that would be fascinating to know, and really valuable to science because there's probably some other genetic gene that's replacing that loss. Or it's compensating in some form.

So we've asked them do you see anybody that has two loss of function variants, do you see anybody that's just a carrier of NGLY1 like me. Are they more susceptible to autoimmune diseases or cancer or neuro degeneration or peripheral neuropathy. The problem is that these companies are desperately trying to make money. 23 and Me has raised a lot of money, but really has not been able to show much revenue ... they show revenue, do they show much profit? No. So we're kind of low person on the totem pole. But they've all been very accepting and very eager to help. It's just companies have this sort of friction point, and that's ultimately one reason where we felt like we'd better start our own pharmaceutical company where we're at control of our own destiny.

I think if anyone's trying to get pregnant, I would definitely do 23 and Me. I would definitely do Council. I would definitely do these services for sure. Do them all. If you can afford them, in many cases insurance pays for them, like Council. So I would recommend it.

Audience: [00:40:00] It's also just good to know for yourself.

Matt Wilsey: Yeah. They're good to know for yourself. There's a lot of people, who, you'd be amazed, a lot of people I come across do not want to know. They don't want to know if they're susceptible to Parkinson's or you know Type 1 Diabetes or anything else.

Audience #4: So I've got a quick question on leadership and culture. As an entrepreneur you've made several organizations. I've personally worked at organizations making innocuous enterprise software and people were freaking out as if lives were on the line. Culture was rough. I've had the pleasure of being at the annual retreat, where a working session of these scientists gather together and it was incredible how positive the culture was. Lives are on the line. These are people who are very busy and have very hard jobs. Along with everything else, how do you keep a place with that vitality.

Matt Wilsey: It's so interesting. I've actually been thinking about it. I'm a big Golden State Warriors fan, and I think about Steve Kerr and what he does and it's so weird because it almost feels like magic in a way. Like I don't know exactly what we do to instill that in people, outside of just treating them with respect and letting them own their work. The only things we ask for are that they collaborate with each other. So we feel like we've built this sand box and it's like everybody in, lets have some fun. We try and make it fun.

Randall Ussery: There's a commonality of them being patient-centered too.

Matt Wilsey: Yeah and partly I think that's part of the vetting process. Will this person be a good culture fit? And it goes back to them taking it and sort of shaping it in their own vision too. We're comfortable with that. It's like, yeah, this is not a dictatorship, this is our community. They are like family. That's how we treat them. I just feel like you create that environment, and they reward you even more so.

Audience #5: On a less business oriented note, how can we help? What do you do to get people involved who are not scientists?

Matt Wilsey: That's a great question. I rarely get asked that.

Randall Ussery: I feel like that's why you asked me all the time.

Matt Wilsey: It's so funny, because originally that's why we created the foundation because some family and friends were like how can we help. And there was really no way that they could technically help outside of financially supporting us. Some of the things we're looking for now are, we're looking for writers on our website, we're looking for people that can help us with social media. We're looking for people that can help us with our events and making them successful.

This summer, we're bringing together all the families, worldwide effected by this disease. So it will be the first time that all the patients will be together. We have families from Northern Israel coming, we have families from China coming. All over

Europe, all over the United States. It will be pretty amazing. Yeah, I guess we also need translators. That's another way we need help. Not all of them speak English.

[00:43:30] It's just also kind of getting the word out amongst your network. When I go on Facebook, I kind of get down because I'm like man, people are complaining about a lot of stuff. And some of it seems so trivial compared to ... and thankfully we're financially OK that we can focus on this. But there's a lot of families that are suffering from some really terrible diseases. Not just in kids, and they're not necessarily rare diseases either, but it seems like a total whitewashing of that fact.

We feel like it's kind of our duty to educate the world, like, look, they're are a lot people suffering. In some ways we feel like that might be why we got Grace, is that we could do this and we could make a difference for a lot of people.

Randall Ussery: And advocate for them, right?

Matt Wilsey: Yes, advocate for the people that can't speak for themselves. For sure.

Randall Ussery: I mean if we go back to the statistic of 80% being divorced, right? Rare disease parents being divorced, then you're dealing with a single parent issue.

Matt Wilsey: I literally don't know how I could it as a single parent. There's no way. No way.

Audience #6: For the geek question, can you talk more about the ... you mentioned that this platform can be used to identify or validate your target. How do you apply the same platform for diseases that are totally unrelated.

[00:45:00]

Matt Wilsey: Some of the examples that we feel are closely related ... various mitochondrial diseases, some CDG's. Sorry, he's a glyco-biologist, so he understands a little of this. CDG's are congenital disorders of glycostulations, so that's the adding of sugars. In our case, it's the clipping of sugars, taking sugars off.

Some of the diseases that are most closely linked are metabolic diseases. In terms of mitochondria, we could do an assay on the mitochondria to see is it improving in

NGLY1? Is it also improving in Rhett's syndrome. So it might not actually be the primary gene that's defective, we might be looking at a secondary, or tertiary target that could give us a readout that the compound is working. If we know it's safe and it's responding in either animals or cells, we're going to push forward on getting it into patients. In those diseases. So in the case of NGLY1, we think probably there's about 8-10 rare diseases that are closely linked to NGLY1.

And back to that number I gave earlier - 200,000. If I add those 8 together, it's about 325,000 patients in the United States alone. So this is where you can build a case for a pharmaceutical company. Now, will all those diseases actually link? Unlikely. But what if we got 2 or 3 of them. It would be quite valuable.

Audience #7: Could you talk about your decision to make a for profit entity and the sort of opportunities and challenges that have come with that?

Matt Wilsey: Oh boy. Yeah.

Randall Ussery: Only opportunities.

Matt Wilsey: Yeah, only opportunities. Well, I'll start with the challenge because it's easy, right? There's two challenges. One, I'm not an MD, I'm not a PhD. Two, I'm biased. My daughter is potentially one of our customers. So that's why it's important to have great leaders around you and also a great board that's independent. You have a scientific advisory board and you have a proper board of directors like any company would. Those people keep you honest, and if I need to recuse myself, I will.

I've told our investors I'm very happy stepping away from the company if that's what they'd like. Of course they don't want that because I'm the fuel to make it go right now. I'm the cheerleader. I'm the guy that's putting the team together. But at a certain point, I will run my course and someone else that's better at this should take it over.

Of course the other challenge would be that, are we going to charge people for an NGLY1 drug? So you're a dad dealing with NGLY1, your child has NGLY1 and you're going to charge us for a therapy. It goes back to that simple Econ101. We have to make money in orders to give the investors a return, in order for investors to invest serious capitol to accelerate drug development, we got to give them a stake in the business, and we got to charge people. But I think the way insurance has been going so far on these ultra rare diseases, they're reimbursing these drugs.

I don't like people taking a drug that's 50 years old and than jacking it up 5000% percent. That's obviously unethical. But in the case of something like this, therapy will not be developed unless we charge hundreds of thousands of dollars most likely for this therapy. It's just simple supply demand curve.

Randall Ussery: Then potentially the foundation shifts it's model, right?

[00:49:00]

Matt Wilsey: It could, yeah. And the opportunities are we really have the ability to work much more efficiently and nimble than anything else that's out there right now. When people say you can't do neuro degeneration and cancer simultaneously, it's like, well watch us. Because that's exactly what we're going to do. And I think it takes an entrepreneurial mindset to think that way. We're outsiders, but we're also insiders because we have the people that have been through those fires before.

Audience #8: Thank you for coming out by the way. It's a super inspiring story. On a more loaded question, how do you feel that this experience has changed you as a person?

Matt Wilsey: It's a great question. Honestly, I've always been a very optimistic person. I feel like I still am, but this experience has made me darker. And that's maybe not a bad thing. It's thickened my skin. I mean, I did, as Randall said, I started my career in Public Service. I worked for President Clinton and President Bush and Secretary Rumsfeld. If you're kind of behind the scenes, you don't really need to have thick skin. We're very much out in the open right now and we don't have an army behind us. You have to develop thick skin.

And ultimately I wanted to get back to being a tech entrepreneur, that's what I wanted to do. So the quickest path to get back to where I felt like I belonged is what I wanted.

But there's no going back I don't think at this point. It has definitely changed my ... I think my purpose in life is to hopefully cure Grace and her fellow patients and then to move on to the next disease and cure those people.

Randall Ussery: I think a big thing too, I mean just sitting on the outside, you haven't done it alone. You've created this support network around you that's pretty amazing. That everyone should think about at some point. You're not going to do it alone, particularly in this field.

Audience #9: You guys were just talking about the power of community. I'm curious if Grace Science is doing anything to partner with the medical community in the way of patient education and advocacy. I'm speaking from experience having gotten a prenatal disability diagnosis for my daughter and they just give you facts. Scary facts that might not necessarily be true.

[00:52:00]

So I'm curious if you're doing any work around how to educate medical practitioners around, here's what we're learning, here's how to talk about it and here's how these parents can get connected with other parents to talk about what I could be like and what life is actually like everyday?

Matt Wilsey: That's a great question. We've been thinking a lot about this, and mostly it's been one off like with GI specialists or a neurologist. It's hard to get the message out to everybody. We've thought about videos. Could we do a video, you know, continuing education. I have clinicians call me from major pediatric hospitals that say I have a patient that was just diagnosed with this. I know nothing about the disease. What can you tell me before I meet with them. I'm thinking, “Oh my God, they're like relying on me?” I mean, I guess I am the subject matter expert I the world now, but I'm not medically trained. So it is a real pitfall.

By the way, the problems will only get worse. So 7,000 rare diseases goes to 14,000 rare diseases. Then what do we do? I mean, we're really going to be drowning. But somehow there has to be like a continuing education loop, be it like videos … no person can read all the medical literature. It's impossible. If there was relevant, if there's a clinic that specializes in movement disorders, like here are the five diseases that were discovered this year, and this is the tell tale sign of them and these are the things you need to be watching out for.

Randall Ussery: And as a parent, you're just increasing anxiety, you're like, “Uh, I don't understand it even more now.”

Matt Wilsey: We had a patient that was diagnosed last June, had made no contact with any of our researchers or us as the foundation. Had not gone into Google and searched NGLY1 and we found them by ... I just cold emailed doctors. Do you have anybody that fits this phenotype, these physical characteristics? Sometimes we get a yes, most times we get a no. This time we got a yes.

I said, can you please connect me with this family. The family didn't even understand how it was inherited. They didn't know that it was two bad copies, on from the mom, one from the dad. How do we prevent it in the future. They didn't know any of that. So it is kind of a scary gap.

From our standpoint, given limited time and resources, we can't answer all those questions, but we do work with rare disease organizations to try to get the word out. Organizations like NORD and Global Genes and Genetic Alliance, Every Life Foundation. So those are a few that act as more of a kind of umbrella organizations.

[00:55:00]

Randall Ussery: The hospital level of thinking about how to get better education.

Matt Wilsey: Oh yeah, within the hospital. I mean within like Stanford, where I spend a lot of time, we think that quite a bit. About how we can disseminate information that's valid. The number one thing that we were told early on is don't go on the internet. That was when Grace was undiagnosed, I mean you just ... it becomes all consuming. So I'm just going to rely on what my doctor tells me and as long the doctor is available, which is also part of the equation, is the doctor or genetic counselor or nurse available? Not always.

Randall Ussery: It's just nice to know ... I mean one of the things you did for me is, our entire family didn't understand what we were going through and so you were like well if you're doctor's not providing you information, it's OK to go outside your network and go to another doctor. Maybe go to the East Coast. Just that simple moment of that I wasn't receiving on the website, or any website, that changed our attitude towards life.

Audience #10: I had two related questions. One, in the news you hear these discussions about Right to Try laws or that approach. I'm curious as to your opinion about those, and if it's going to be effective. And then related to that, where does the US stand globally in terms of scientific progress? Are there other countries where you think Grace might get help before a treatment's available in the US?

Matt Wilsey: Two great questions. On the Right to Try, I'm all for allowing families to make that decision to try a drug. Especially one that we know is very safe. It's already gone through it' toxicity studies, it's in other patients. There might be some sort of bad luck where that particular drug just really is lethal or causes major consequences in a disease that they didn't really test for. People that are doing the right to try typically have no other options. They're really at the end of their rope. Life is pretty bad.

In our case, people asked me all the time as we were starting this company, will we be pushing just for tox studies, or will we also push for efficacy. We're going to be pushing for both, like any legit pharmaceutical company. We're going to run this like Pfizer in the sense of it better be safe, and it better be effective. And if it's not those two things, we're not going to send it to the FDA.

In terms of the US vs. the rest of the world, I still think the US is the place. We are very fortunate that we are here and that Grace was born here. There is cutting edge research that is happening all over the place. Japan, China, Germany. The fact is the top post docs in the world want to come to the United States. So we have the best talent.

I just think that this is ... there are all the negative things that we talk about right now around what's going on with NIH and other things in terms of budget, but this is still the place you would want to be if you wanted to develop a treatment for a rare disease, for sure.

[00:58:30]

Randall Ussery: But you haven't limited yourself to here?

Matt Wilsey: We're in six countries, I should also mention that. Yeah, we're supporting people in six different countries. We're amping up some stuff in Japan right now, so we'll be doing some cool things. The scientists that discovered NGLY1 25 years ago is based in Japan. We have a significant research center there and then also in Germany. In Heidelberg.

Audience #11: You've mentioned some challenges that have been faced through the processes that are already in place with the government, with academia and all of the red tape that's there. How do you see switching over to ... or focusing more on that for-profit side of things with the controversy around the genetic modification, or treatment of humans? Since like designer babies.

Matt Wilsey: Oh, in utero?

Audience #11: In utero especially, but I mean ... I guess yeah, mostly primarily there. How are you planning on tackling those challenges or is that something of a more of a like, we'll get to that?

Matt Wilsey: Like will it be different as a for profit vs a non profit?

Audience #11: Versus a foundation where as a foundation you get that warm fuzzy feeling, so you're less likely to be, “That's wrong.”

Matt Wilsey: I can tell you that people treat us like we are a for profit already. If we tell a researcher that we're passing on his or her grant proposal, they give me an ear full. They have no concept that I'm a dad affected with a rare disease. That literally I look at the customer, the patient every single day. It all goes out the window. So people treat us ... I would say they're threatened by us, and I would say that typically is a good thing. It they're threatened by you, that means you're changing things, be it a for profit or a non profit. So I think that from a for profit stand point, we're going to hit these things head on just as we've been doing. I don't think really much changes in that sense.

Randall Ussery: I think the big deal is you're always going to be warm and fuzzy and you're going to be outcomes-based.

Matt Wilsey: Yeah.

Randall Ussery: And neither two do you have to give up, right?

Matt Wilsey: Well I don't think we have to give up on either of them. We won't shy away and I don't know if we get much of the halo from being ... like if the foundation does from like the government or from pharmaceutical companies.

At the end of the day, it goes back to my experience in business development, which is like if you send someone a sincere, honest note asking for feedback or help, assistance, it doesn't matter if you work for the president of the United States, you run your own pharmaceutical company, you run a tiny nonprofit, if the message is good 99 times out of 100, you're going to get a response, and you're going to get a meeting. I don't think the mechanism of the for profit or the non profit changes that.

Randall Ussery: Well thanks so much for that. We really appreciate it.