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[CLICKING]

HANNA
ADEYEMA: OK. Thank you. Thank you again for doing the work, the reflection, and trying to engage your mind and hand in this activity. Next, coming up is the Prapela case study, our first session. Erdin is going to moderate it with the actual CEO of Prapela, John Konsin. And what we'll do for this, we are going to have a very interactive, no slides workshop. You have all received the case-- brief description of the case study. Hope you had a chance to look at it. And we'll just set it up in a second.

ERDIN
BESHIMOV: That's great. Thank you very much. Can we proceed with the case study? Yeah? OK. Great. John, thank you so much for being here. You may not know this, but the students here know you already through the case study. So here's why we are doing it. Let me just make a few remarks. And John, you can make yourself-- yeah, please.

All right, folks. So here's the deal. Entrepreneurship is neither science nor art. It is a craft. And in a craft learning from mentors, learning from leaders is essential. This is why we are doing case studies. They're going to be very interactive. The goal is for you to express what you think, to argue and debate. Expect cold calls.

So we do expect you to have read the case studies before the case presentation. So be ready. And the reason we're beginning with this case study is this. Let's make no mistake about it. The field of addiction doesn't provide a lot of hope for us at the moment. And I think that's just the reality of it, that we cannot yet say that there are solutions that are going to be-- certainly be able to address those problems within the space of this perhaps hopeless stasis.

And that's what it is. And so as we were designing the program together, one of the things that we were asking is, what can we do to give people hope? Because entrepreneurship and innovation begins with hope. And when we learned about Prapela and what John and his team are doing, we just said, oh my God.

This is the way. What a great case to really bring to life the importance of hope. That's number one. And number two, really, there is a lot to learn from this case study about how technologies get commercialized, how leaders steward those technologies. Thank you. Thank you very much.

Let's begin. Marco, may I please summarize-- have asked you to summarize part A of the case where the background of John is described in the health care field. Have you read the case? OK. That's fine. Who has read the case? Raise your hand. Yeah. Sarah, please. Will you summarize John's background, how he came into the health care field?

AUDIENCE: Sure. [INAUDIBLE] so [INAUDIBLE] see the best I get. John is someone who has really started in corporate America. So large organizations where [INAUDIBLE] it is 3M, essentially [INAUDIBLE] company. So Peter Products, sticky notes, but also has quite the health care arm as well. And so looks like how did this gained a track record through that preparation to really focus in health care, which is where he started career and really started [INAUDIBLE] in solely on health care and developments on [INAUDIBLE].

ERDIN That's fair. That's all fair. And so the goal is going to be we're going to go through a set of questions to set up the case, and then John will offer his reflections on your comments. That's going to be key. And then we'll have a Q&A with everyone in the group. Now. So as you can see, John is coming into this field, into a startup that eventually became Prapela from a corporate background. Now, Mark, if I could go to you for a second.

You are going into the field of SUD entrepreneurship from the academic field. You are a faculty member at Rockefeller. You're spinning out your company. How do you think your pathways-- well, your pathways are different from John's, even though you are, in a sense, ending up in a similar destination? But how do you think how you think, what the skills you have, how you think about the world, how is it different from John's?

AUDIENCE: I think they're probably 100% different.

ERDIN Actually, here's a mic.

BESHIMOV:

AUDIENCE: I think they are probably 100% different. I'm coming from the molecular mechanism aspects of it. Not so much from any business development side. And I feel like I understand the basics of what needs to be done but not probably how to do it. And I hope I will make progress on that quickly.

ERDIN OK. And so how do you think about it in your company right now? What skills do you acquire by bringing additional team members? What skills do you need to nurture in yourself as the entrepreneur leading event? And that's an important question for all of you. Here partly you are to meet others so you can identify additional skill sets. You're also to grow yourself. How do you think about it?

AUDIENCE: Well, I definitely need everyone that is focusing on different aspects than just the research itself, basically. I will need advisor. I will need probably at some point a CEO that has experience in the field, ideally in the field of health care, and then maybe even more in the field of SUD, if possible.

ERDIN Why? Why would you like a CEO instead of you being the CEO of yourself?

BESHIMOV:

AUDIENCE: Well, because that's not what I would do best. Maybe I can try it, but I don't think it would be efficient for the company to be fast, to be-- yeah, to be moving as quickly as possible.

ERDIN OK. Now, who would like-- thank you. Who would like to summarize part B of the case where the technology is described? Please.

BESHIMOV:

AUDIENCE: Thank you.

ERDIN Yeah.

BESHIMOV:

AUDIENCE: My name is Tomoko. Nice to meet you. So the B is about the scientist discovering-- made an observation, which came to an idea where it could channel into the-- sorry. I'll take my notes.

ERDIN It's all right. Take your time.

BESHIMOV:

AUDIENCE: Into the baby suffering from irregular breathing. And this Dr Paydarfar, he--

ERDIN John, did she say it right?

BESHIMOV:

JOHN KONSIN: Paydarfar.

ERDIN Yes.

BESHIMOV:

AUDIENCE: He really narrowed into the interest that he discovered, and he found a niche, which was the opioid exposed babies. Yeah. And there was obviously a need, an unmet medical need in the research that he has continued and he developed actually a medical device that have seemed to give results in the experiment. It says experimental, so I'm guessing it was some kind of clinical trial or something that they did. They actually seen a positive effect on the medical device that he made. And then he made the connection with John, who has then-- yeah, wanted to make this into the market.

ERDIN Right. But I'm going to push this a little further. What does the--

BESHIMOV:

AUDIENCE: Oh, yeah, I also wanted to highlight what I think is really interesting alignment on scientific advances. The point about serendipity and observations with this way, which really actually made science into the results from the health applications. Other famous examples are [INAUDIBLE] and observation and something going on. Like, them really crystallizing everything.

ERDIN That's a great point. Now let me push again on the technology [INAUDIBLE]. One of the things we're learning in
BESHIMOV: this book is, in general, that technology [INAUDIBLE]. So firstly, describes it in ways that are simple, understandable, also comprehensive. So what does the technology do?

AUDIENCE: So-- eh.

AUDIENCE: [INAUDIBLE]?

AUDIENCE: Yeah.

AUDIENCE: Oh, well. So basically, stochastic resonance, and the idea of using that as a signal amplifier. Yeah. So leveraging that technology in combination with some of the discoveries in biology in relation to the squid and what was observed in a completely different area of expertise and connecting those dots together in order to leverage that in a way that can be used to help treat substance use sufferers. Yeah.

ERDIN OK. Good start. Now, let's do this again. Hey, if I'm pushing this as purely for the goal of learning the goal.

BESHIMOV: There's nothing else going on. This is a goal. But put yourself in the shoes of Dr. Paydarfar. Right? You've identified this interesting phenomenon. You're fascinated by it. You've also been working on it for a number of years. You've been working 15 years. So there is something new that you care that it goes somewhere.

And it is important for you that someone like John gets interested. So you need to find a way to date, in a way. John is not a scientist. He's been around technology, but He's not a scientist. We need to explain it to him in a way that can dispense, and more importantly, he feels compelled by it. Right? So let's then describe this to John.

And what John is going to do, he will tell you how Dr. Paydarfar presented everything. Because there is a reason he got interested. And one of the reasons is Dr. Paydarfar and how he describe it. So let's-- oh, do you need the mic? Yes. No. Yes, yes. I will be using it. I'm sorry. Yeah. No. So, Tomoko, you go, and then let's go with you again. Yes. And then-- sorry about that. Yeah. We don't have [INAUDIBLE], do we?

AUDIENCE: We do, actually.

**ERDIN
BESHIMOV:** Yeah. Oh, there. Yes. Yeah. So let's do it. Let's describe the technology in a way that raises the interest and is understood.

AUDIENCE: So this technology, the signals are very weak, and usually it's too weak for normal devices to pick up. So it's impossible to measure these. By utilizing this particular technology, you can amplify it, as Corey said, and put it in a form where it's very easily detectable. And that's powerful because you're putting from impossible into something that's realistic.

**ERDIN
BESHIMOV:** Boom. Right? Everyone, observe. She's saying that was impossible before. With this innovation, it is all of a sudden John is interested. What he needs to know now is that that impossible thing is also valuable. Do you want to give that a shot? Right? So not all possible things are valuable. Why don't you give it a go? Yeah. That was good. Impossible is now possible.

AUDIENCE: OK. Let's see. Can you reframe that one more time, please?

**ERDIN
BESHIMOV:** So what Tomoko said, she said, hey, signal amplification of the sky was impossible before this technology. And if I'm speaking loudly, it still doesn't help, right? Because--

AUDIENCE: No. I need the--

**ERDIN
BESHIMOV:** OK. Could I use the mic just for me? Right. What Tomoko is saying. Hey, there is this interesting technology that we've been working on for a long time. And by the way, this is not just in our field. This is now a general phenomenon that physicists are aware of, that biologists are aware of. So it's real.

And signal amplification of this kind was impossible before. It is possible now. So John is interested. Huh. Something that was impossible is possible now. But he needs to know that this is valuable as well. That there is value in signal amplification. What do you say to him?

AUDIENCE: So there's this idea of stochastic resonance has been around for a really long time. It's a proven technology and it's a proven way of amplifying signals that are otherwise undistinguishable, like in the noise. And that's something we can apply to many different problems and can capitalize on on some further investment.

**ERDIN
BESHIMOV:** OK, good. All right. Do you want to give that a go? There you go.

AUDIENCE: Thanks. So my name is Gifty and I just wanted to add on that, at least in the case study, it mentioned that current technology. So with the stochastic resonance, it was used to help with motor functions. So that was one evidence of why that technology may work.

And then, as you referred to earlier-- I forgot the name, but it did mention how-- was it Corey? Corey, yes, with the vibrating insoles. So that's all examples as well as the squid reference that was made. So that's all evidence that there's somewhere-- you can go somewhere with this technology.

ERDIN BESHIMOV: Yeah. All right. So now Melanie, let's go to you. Thank you, Gefte. So Melanie, you are now John. And you're speaking with Dr. Paydarfar. You've heard about this tech. You want to ask questions. What questions do you ask Dr. Paydarfar? Because your mindset is not purely scientific. You're wondering, hey, can this become something commercial? What are the questions that you ask?

AUDIENCE: Sure. Good morning. My name is Melanie Jimerson. I think in a response to a question I'd ask, I would first start with the mindset. And the mindset is that progress is not linear, but it's more of a momentum or continuum of everything that we're continuing to work on. And so I would ask next is, for this viable idea, how could we continue the continuum of the progression of the technology that we have? And in what skills? Yeah.

ERDIN BESHIMOV: So how will the technology develop? How will the tech develop? Other questions. How will the tech develop?

AUDIENCE: Hi. I'm Dr. Ray Denny. It's nice to meet everyone here. Other questions I would ask. How reliable is this technology? If we're going to be administering it to the premature babies, it has to be reliable. Also, it has to be reproducible.

ERDIN BESHIMOV: Define reliable. Reliable in what sense?

AUDIENCE: Reliability. When it's detecting the signals, how likely is it to detect the correct signal? Basically, how safe is it? Is it reliable? Is it safe?

ERDIN BESHIMOV: OK. Safe. Other one? OK.

AUDIENCE: How can it actually be deployed?

ERDIN BESHIMOV: How do you mean? Manufactured? Marketed?

AUDIENCE: Manufactured. What is it going to look like that's usable? So even if--

ERDIN BESHIMOV: That's your job as John. Dr. Paydarfar doesn't know the answer to this.

AUDIENCE: Oh, OK. So he wouldn't be asking the question.

ERDIN BESHIMOV: Because if you as the business person go to a science person and say, hey, how will you take it to market, you're not fooling around [INAUDIBLE].

AUDIENCE: I'm not asking how you take it to market. I'm asking, what is the vehicle for this technology to be actually introduced into the real world. So the technology is there. They put it into a bassinet. So I think the question would be-- but I mean, I'm assuming that this came to John before the bassinet was fully developed.

ERDIN How do you product-ize it.

BESHIMOV:

AUDIENCE: How do you product-ize it. Yeah.

ERDIN We're making this technology be-- OK. I got you. That's fair. How would the tech be deployed, in this sense. Yeah.

BESHIMOV: We'll go to you. [INAUDIBLE]. Mark.

AUDIENCE: One of my questions is, how is it differentiated? In particular, you have vibrating solutions, random noise generators that are available in a consumer goods space that have no regulation associated forum. So what are the discoveries that have been made that could differentiate this and apply this through to warrant the additional costs and overhead required to make this into a medical device technology?

And then this leads directly into the question about intellectual property. What about this resonance or particular form of resonance is going to be optimizable or going to be patentable, such that it's not obvious to anybody who's been developing bathing soothers that were already in the market at that time? Such that there is a moat formed through intellectual property.

ERDIN OK, right. So now you're introducing IP. And what we need to start thinking about, all of us, is John is already

BESHIMOV: thinking-- when he is hearing all that, he is thinking, who do we need on the king? We need IP. Who are the right folks to go to for that? We need manufacturing. So we need to start thinking about team composition. OK. Back [INAUDIBLE], coming to you. Thanks, Mark.

AUDIENCE: Perfect. He already said my two points really, which were from a regulatory perspective, what are the predicate devices that you would be referencing in filing a 510(k) so that the FDA can understand hazards and efficacy are the only two things the government-- I mean, are the core foundational issues. And then on the intellectual property landscape, it's just vital to spend dozens or hundreds of hours searching the entire IP landscape that could be relevant to this, because the business model has to hinge on not just excellence, but protection.

ERDIN Yeah. And could I actually put you very quickly on the spot? You've been in the shoes of talking about your

BESHIMOV: innovations at MSG to potential licensors of that technology. How did you present those innovations? What high level advice do you have for the folks here as to what's important?

AUDIENCE: That's too big a question, because it depends, I guess, on whether you're starting from the health care organization, and let's say a consortium of neonatal intensive care units who meet regularly and identify long felt needs. And they could be the pulling function to bring the technology into existence as opposed to the technology push, which is from the research labs and companies with a cool new thing. And we always said at MGH, that the magic space, the serendipitous space, is how you match up tech push with clinical pull.

And so that's the high level way that I would think about it, as opposed to just how you would present it. I mean, that's more like, hey, is there a particular neonatal intensive care unit that's very, very interested in certain issues with premature infants and has all-- is eager to be the first pilot site for a clinical trial once we figure out whether this is a 510(k) application, because there's strong predicates, or whether it's a PMA or an IDN, which our friends can explain.

All of those pathways are very complex. And of course, I'm sorry to keep babbling, but there's the institutional review committees for the trials for human studies, which this would be the first-- if one was doing a study of the device in a clinical setting, then you've got to have institutional review board approval. And the IRB is going to say, hey, is this FDA approved or not? If not, then show me that you've done your homework as far as the pathway. So it gets complex.

ERDIN And then to you, Leonardo.

BESHIMOV:

AUDIENCE: I was just going to say some additional questions that haven't really been touched upon. How much does it cost? What's the market size? Are there already patents in place? And who else is on board?

ERDIN Are there patents? Who is on board? OK. Let's go to Leonardo. And then, John, have you come take-- set the stage of the reflections on the perspective [INAUDIBLE]. But Leonardo, please.

AUDIENCE: Very briefly, one question, and then John, I'm sure, will comment why. Why we care about the technology. Is there a problem to solve? And we will also discuss, and John will present. There is actually no predicate, so we have to be a pioneer in creating everything, creating regulation and negotiating with FDA. And that's really suffering. But why we care about that. And then I'll pass it to John.

ERDIN John, please join us here. So I want to make sure there is a great deal of time to interact with you. Welcome, by the way. Thank you so much for being here.

BESHIMOV:

[APPLAUSE]

Doctor, since you raised your hand.

AUDIENCE: Just one other loose topic is the management of conflict of interest to the extent that it's invented somewhere by somebody and you need that person, the inventor, in the startup in order to provide domain expertise, in which case, the management of conflict of interest. If the inventor is a employee of a provider organization like Rockefeller or Mass General, then that's a whole space that has to have a lot of attention paid to it.

ERDIN Would you have comment for that?

BESHIMOV:

JOHN KONSIN: Yes. And several more. So I don't want to start with that. I'd like to start more at the beginning and then jump into this and we'll come back. Is that all right?

ERDIN So yeah. In that case, let me ask you, John. Would you offer some perspectives on the journey that are not in the case that it perhaps offer more to the students?

BESHIMOV:

JOHN KONSIN: Sure. Sure. And in fact, I was taking some notes, so let me reflect on those. What came up early was, hey, what kind of abilities do you need to really get a venture going? And abilities are very important. We hear about knowledge, skills, and abilities all throughout our lives. You need to develop knowledge. You need to develop skills. You need to have abilities.

And I think, synonymous with skills are traits. And starting a venture, whether it's focused on substance use disorder or something else, requires, I believe, first and foremost, a trait of resilience. Resilience. Because nothing goes the way you expect it to go. There will be setbacks along the way. Things that you think are slam dunk are not. You will be surprised.

And it's your ability to take a step back, learn from that setback, and then set a new, more powerful course to succeed. So resilience is absolutely key to the success of your venture in this space and in any other startup space. Got it? Startup. Another trait I'd like to reflect on is actually reflected and written about long ago in a book by a gentleman named Jim Collins called *Good to Great*, who did extensive research on what made companies really successful over a sustained period of time.

He concluded, among many things, that leadership at the top of a company needs to be humble but driven. And I think we've seen countless examples, especially the last few years, where you can say to yourself, this person is really driven, but maybe not so humble. This person's really brilliant and they know it, but perhaps not so humble.

And while they may have great success, it's the companies that endure that are most important to us, the companies that provide innovation after innovation, that return great stockholder wealth but also improve human lives. And the CEOs in lineage of those companies, if they're humble and driven, typically provide and deliver on those kinds of promises.

So traits. Resilience, humble, but driven. OK. Thanks for letting me get that one out. It's all about technology meeting needs. So we're going to talk about Paydarfar for a second. So he's down at Woods Hole and he discovers that every time the table shakes the squid that he's doing the experiment on, the axon fires. And he wonders why.

Why does this axon fire every time the table shakes? And the table shakes because it's trying to maintain a saline temperature bath at a constant level. And to do that, it stirs the saline, and that saline tub is next to the table. And when it stirs, it makes the table shake. But just ever so slightly. And at first, Dr. Paydarfar didn't even realize that the table was shaking, so he couldn't figure it out why.

So this is an important trait too. Collaboration. What did he do? He didn't sit back and just say, well, what could it be? He went to go see another Collins, believe it or not, only this one happens to be at MIT. And he says, I noticed whenever this table shakes, this axon fires. What the heck is it? And Jim Collins, another one, says to him, oh, it's stochastic resonance.

And at this time, maybe stochastic resonance is around 10 years old as a field of science. It just celebrated its 40th year anniversary in 2021, by the way. So it's a 42-year-old known technology now. And Paydarfar says, what the heck is that? And Paydarfar is no dummy. Physics undergrad, MD, Duke, UNC, at Harvard, practicing physician. Now chair of neurology at the Dell Medical School. So pretty bright guy.

But he's humble enough to listen to what Dr. Collins has to say, and he dives in. And he starts his journey of, well, I want to have this apply to helping babies breathe. Now, where did he come up with that idea? Well, it just so happens back in the '70s there were a couple guys at McGill University who wrote some papers on mathematical modeling of human respiration.

And Dr. Paydarfar drew his experience in looking at babies in the NICU, knew that there were breathing problems. And so he thought, well, if I can make this work to help babies breathe, that could be really something. So he did further computational modeling and then developed the very first device. And back in 1974-75, published his first paper with one neonate that said, hey, guess what? This stochastic stimulation seems to work.

Now, he didn't have it all sorted out. He didn't know what the amplitude. He didn't know what frequency. But again, he was humble. He was driven. That led him to work at Harvard and the Wyss Institute, where they developed better prototypes. They did first investigational device studies on humans. They expanded the number of babies that they were looking at and went from that one.

And they did, in 2009, a study with 10 preterm infants and showed, yep, we're actually seeing improvement in breathing control in preterm newborns. Fantastic. All right. So stop there. That's a big important story about, I think, Dr. Paydarfar. Does it help? And I'm going to come back here. We good? Any follow on question about early innovation?

So now we'll go-- so this is the innovation. This is the technology. Now there's the next phase, right? Which is, OK, from technology to, I'll call MVP. Minimum viable product. And Dr. Paydarfar turns explanation up front. Isn't a business person. He's not literally thinking about, well, what is the product? Right?

I know I've got a concept here of this pad that baby can lay down on to improve breathing, but what really is the product? So that's really the second phase of this development. Right? And serendipity with the squid. Love the word. Serendipity for me, right? I just left running a company for four years out on the West Coast that happened to be what was my first experience in electro stim for pain management. Couldn't get the board to go in the direction I want.

CMS had dropped coverage of our number one device, which was TENS, to treat low back pain. They had covered it for 20 years. And 60% of our revenue disappeared in a period of four months. You have 600 employees, and when 60% of your revenue goes away in a very short period of time, you better scramble. You better be resilient. So we did. We got the company, we stabilized it. We survived.

But it was time for me to move on because I couldn't get the board to expand into other areas, other technologies to address pain. Fast forward to the end of 2016. My stepson has an overdose in our house in the bathroom. We discover him blue. Luckily, because he had been going through counseling, we had Narcan in the house. We revived him. He's doing great. He's living in Michigan, happy that he's alive.

A month later, after I'd been working with Harvard on a Microbiome Project, they called me and said, we got this other technology we want you to look at. We don't know how to get it to market. We can't get any of the big companies interested. Why not? You've worked at big companies. Tell us what we're missing. I go down, I look at it. Within a day, I tell them why no company is going to look at it for a while. They believe me.

About two weeks later, impressed with what it could do for opioid exposed babies, Barbara and I, my incredible spouse partner, agreed this is what we were supposed to do. Went back to Harvard, said, I want it. I want to bring it to market. They said, OK. That started the MVP journey. What is the MVP? Luckily, some of the skills that I had early in my career was as a marketing analyst. Right?

OK. What could this become? How do customers? What is the NICU? What is the market size? What is the application? What's the competition? All those things that I learned as a marketing analyst early in my career, I started applying to this opportunity and started thinking about how to bring it to market. I thought, this is going to be easy. I'm going to put together some slides, PowerPoint slides. I'm going to get in front of some angel investors.

I'm living in Boston. I'm living in Concord, Mass. Former CEO, 30 plus years experience in medical devices, Harvard technology with MGH and University of Massachusetts. The three institutions collaborated on it. Got a real market need. I got investigational devices developed. I've got clinical studies, I've got patents. Oh. I'm going to get \$2 million right away after my first presentation or two.

Fail, fail, fail. Angel investors, they're great. They're wonderful. But at the end of the day, they're hobbyists that are looking to make \$40,000, \$50,000 investments, maybe \$10,000 or \$20,000, and they want something a little bit more proven. And they want a whole lot of your equity up front. So somebody told me about how to write a grant. And I'm like, well, wait, how do you spell grant?

Even though he's a former CEO, I didn't really know how to spell grant, let alone write one. So I went on the internet. Oh, yeah. There's these things called SBIR grant? Oh, yeah. I'll write one. No problem. Spent a couple of days. Tossed it in. This would be easy. All the same assumptions I made with angel investors. I get this feedback, I don't know, a couple of months later. It wasn't scored.

Wow. That must mean this is great. It was so good, they didn't even score it. Right? No, dummy. It means it was so bad that nobody even wanted to give it a second look. They didn't even want to waste time discussing your grant application. Oh, man. OK. Angels aren't going anywhere. I'm not getting any love on the grants. Oh.

Start a substance use disorder challenge, NIH, sponsored by the National Institute on Drug Abuse. I think I'll apply for that. \$10,000 award. Applied. Get it. I get the \$10,000, and I'm really excited about it. But you know what? The real benefit is sitting right here in this room. The benefit was, oh, you're going to get to learn how to write a grant. Oh, super.

And we're going to teach you how to do it. And I get on the phone with Elena, and she basically tells me, a former CEO of a mid-cap company who developed a 35-year career with many of the world's best companies in medical devices, is going to teach me how to write a grant.

She lays it on the line. This is going to be tough. You're not going to like it. You're going to do everything I tell you to do. You're going to do homework. You're going to submit it. I'm going to evaluate it. I'm going to critique it. And you're going to write it again. And that went on for six months.

Write, rewrite, write, rewrite, write, rewrite. Submit the grant after it. Wasn't perfect. It wasn't a really great score. But I got scored. And I got NIDA to step in and give us our very first grant. Amazing. This set the foundation. To date, we've won over \$8 million in non-dilutive awards and grants. Yeah.

[APPLAUSE]

And taking exactly what she told me and working at it year after year after year, the last grant I applied to was scored an 18. And we'll know in a couple weeks if we've got that grant. And if you're not familiar with grant scores, they go from 10 to 90. Lower is better. Usually 30, you're in the ballpark to get funded. So getting an 18 is pretty darn good. Going from not being scored to 18 is fantastic.

So why do I bring up this important element? Because in order to go from an idea and a technology and investigational devices to an MVP towards commercialization, you need money. And there, in my opinion, my humble opinion, there is no better source of funding for a startup in this space than the NIH and NIDA specifically.

This is absolutely America's seed fund and the support that you receive-- and by the way, I'm not getting paid for this. Nothing on the side. All right? Is immeasurable. As long as you remember to stay humble but driven. What is non-dilutive mean? It means that you're not picking up the phone every week and talking to 10 different investors who are saying, why aren't you moving faster?

It means that you have time to think about how you're going to go to market. It means that you have credibility when talking to physicians that are interested in using your product or your technology. It means that you have something to show to people struggling with addiction. That there is a promise that you are working on something that will help resolve an issue. That is really what you get.

And oh, by the way, after you get these other things sorted out, it's an incredible backdrop to investors. It's proof. It's a proof source that you know what you're doing and that you have a path forward towards success and you've been successful in the past, and in all likelihood, you'll be successful in the future. It's a fantastic proof for source to get grants.

By the way, you can't answer these questions really, really well until you write a grant, because you've got to answer all these questions when you apply for an SBIR grant. All these things that we talked about. What's your price? What's your go to market? What's your IP? What's your cost of your product? What margins are you targeting? How big is the need?

What's the adoption rate? What's going on with reimbursement? What's going on with regulatory pathway? You have to understand all of those. And in my opinion, humble opinion, is the best person to write the grant is the person that's leading the company. I can't tell you how many people called me up over the last two years. Oh, I see you've done really well with some grants. Who do you use?

And I go well, I write them. No, no, you don't write them. You're an MBA from the University of Colorado. You don't write them. Come on. By the way, when I went to Colorado for my MBA, we used to say it's the best MBA program in the Rocky Mountains. Try and name another. OK? So, yeah, I can't tell you how important it is to develop that skill in writing grants and how valuable it is.

It's not just about securing the funding and the relationship. It's also what you learn when you realize oh, I've got to write about this. Now I've got to write about innovation. Oh, I've got to write about significance. Oh, I've got to write my commercialization plan. I've got to write about my team. I've got to write about our facilities. And you've got to write it in a convincing way so that you get a low score. All right. Go.

ERDIN
BESHIMOV: So the moment that I want to ask you about is Dr. Paydarfar approaches you. What strikes your interest? Why are beginning to think, hey, this is not just a great technology, this can be a product? And what's more, this can be a successful business.

JOHN KONSIN: So the quick answer is, oh my gosh, you're talking about something that a baby lays down on and it helps them. Gee, babies lay down a lot in hospitals and at home. This could be amazing. All right? It was one of the first opportunities that I saw in my career where there was a potential medical to consumer crossover. That really got me excited.

Also, the evidence that they had developed. The link between here's the technology and the explanation of the mechanism of action for that technology to the results that they were seeing in investigational studies. All right? And to be clear, what we're doing is we're talking about what stochastic resonance does at this level. Because it's not just generic stochastic resonance.

It's for, in this application, at what frequency, at what amplitude? All right? We're talking about a randomness in terms of the up and down movement, which, by the way, is less than half the diameter of a human hair. I brought a device for you to see it break so you can feel it for yourself. And you're talking about a randomness in a frequency bandwidth, the speed between 30 and 60 hertz.

And it randomizes in that speed, and it randomizes in the up and down movement. And that is the brilliance of what Dr. Paydarfar discovered. It was that stimulation at that level which actually improved breathing. And he discovered that, yes, it started with the squid, and also he proved it computationally through mathematics, which I can never do. Please.

AUDIENCE: Said that said no, [INAUDIBLE].

JOHN KONSIN: Yeah.

AUDIENCE: Tell me about why you said no.

JOHN KONSIN: Yeah, yeah. So why did I say-- well, some of it had to do with whether or not I was even really ready to. I mean, at my age, after my career, most people say, yep, time to cash in, join the country club, play golf, hang out. And I knew that even if I were to secure some investment right away, it was going to be a big hardship, potentially, on my family. So that was a big, big element of it. Right?

The other element was I didn't feel that the clinical studies were robust enough to take me to clearance as fast as I want. By the way, point of clarification. All right. We discovered during our journey that it's not 510(k). It's a de Novo. Right? A de Novo is not a 510(k). A de Novo means what? New to the world. New.

So the FDA says we want all this safety testing, non-clinical and clinical, and we want efficacy. And we want you to present this to-- obvious. And I was feeling like I didn't even know it was going to be a de Novo. I thought it was going to be a 510(k) plus clinical studies is what I thought initially. By the way, resilience. We applied for de Novo in April of 2023.

They said no. FDA said no because the clinical study that we used was too small, they felt, and we knew we were at risk. And they moved the goalposts on cytotoxicity testing from a qualitative test to a quantitative test. And by the way, there's an bassinets pad in the US now in any NICU that passes the new test. But that didn't matter to them. They wanted us to pass it. And that's OK.

A month after the FDA told us no in April 2023, they knew another study was coming out. The study was published in *JAMA Pediatrics*. 181 newborns. And what this technology does is it reduces, as shown in the *JAMA Pediatrics* study-- which is what we're submitting with our new de Novo, soon to go in-- is that it reduces the amount of morphine that is required to help calm these babies. In fact, over a 21 day period, these babies need 44 less fewer doses when they're on our pad.

That's two a day fewer doses of morphine to calm them down. That's a good thing. It reduces their length of treatment as well. And we're just about to start analysis on a new study that we completed at Tufts. There wasn't one baby who started following birth that was on our pad that was ever treated or ever required treatment with morphine. So a different study than the one that was just published in *JAMA Pediatrics*, which, by the way, started five years ago. So those are two principal reasons. Thanks. Great question. Please.

AUDIENCE: One of the things that I noticed in the case study was kind of the burden on the hospitals. So my twins were in a NICU. I experienced firsthand the craziness that the staff deals with. So I'm curious, was there any-- when you guys were going to these different institutions for the clinical studies, what was the response that you got from them?

Was there are a lot of pushback with a concern of uptake? Because that's generally a big problem. And did any of the studies also look at who was their decreased resource use? Like, were they discharged from the hospital quicker? Were any of those things?

JOHN KONSIN: So everybody got the question? It was basically infants that are exposed to opioids after birth as they experienced withdrawal, which is neonatal abstinence syndrome, sometimes called neonatal opioid withdrawal syndrome, placed a heavy burden on the staff at hospitals. So what did we investigate? What did we find? What were hospitals saying about the situation?

Well, I'm going to go back to the very first grant, right? Which was an SBIR phase one. And what does an SBIR phase one do? It tells you, you need to tell us two things. You need to tell us, is your technology feasible? Can it be reproduced? The question over here. Can it be done accurately? Can you produce a device that's going to consistently perform the way it needs to develop and provide the efficacy that you think it provides?

And the second part of an SBIR phase one is, what's the commercial feasibility? And the commercial feasibility goes right to the heart of what? The users of the product. Babies. But in this case, because they can't really talk about what they need-- they do cry really well, though. But their caregivers at hospitals could explain to us what the burden is in caring for these babies and whether or not our device had promise in helping them with the burden that they had.

So during my phase one grant, that's what \$222,000 gave me the opportunity to do. Technical feasibility and commercial feasibility. As part of the commercial feasibility, we did several things, but I'll just reflect on one experience. I went to Baystate Medical Center in Central Massachusetts. I spent a day with the head of the neonatal intensive care unit and the pediatric physicians there.

And the day ended with a two hour session in a nice room where we talked, and they also did surveys. Completed the survey before we did our talk, et cetera. And there I met Dr. Rachana Singh. The feedback was incredible. They told us that they would love something like this to help them care for their opioid exposed babies, which was a big issue to them.

And they explained what the burden was, and they explained how constantly they had to hold these babies and how the morphine doses for some babies was just burdensome, et cetera. Which is all great and good. You get that in the surveys. You got that information. But it was the end in the hallway that mattered so much to me. Dr. Singh came up to me and she looked at me and she said, whatever you want, however I can help, just let me know.

Fast forward. We get another grant. We're going to do the study at Rainbow Babies Children's Hospital in Cleveland. The head of the NICU leaves for a position at the NIH. They can't do the study because the new head of the program can't do it. I need to find a replacement. Literally where am I going to have the study done that we had gotten basically the go ahead from NIDA to do?

I call up Tufts Medical Center because it's in the backyard here for me. No, I call Baystate. Dr. Singh, she's going to help. Well, she's no longer here. Where did she go? Oh, she went to Tufts. Oh, OK. Call Tufts. There's Dr. Singh. Sure, we'll do it. Relationships, collaboration, support. Those are the things that you just need to stay on top of. So long-winded answer. Apologize.

In the studies themselves, the *JAMA Pediatrics* looked at length of stay. It looked at time on crib. It looked at morphine doses, cumulative morphine doses. On the new study that's going to be published in the next year coming out of Tufts, it's going to look at length of stay, length of treatment, and whether or not any babies were-- their symptoms were so severe they needed to be treated with morphine. And as I already kind of sold it a little bit, I know, just at a very high level, we didn't have one baby move on to morphine treatment at Tufts, which was amazing.