# Essential Tips for First-Time Medtech CEOs: Interview with Dan Rose, CEO of LimFlow

**Scott Nelson:** I recently had the opportunity to interview Dan Rose, the CEO of the French-based med-tech company LimFlow. Founded in 2012 LimFlow has transformed the peripheral vascular space by providing a lifesaving option to patients suffering from C LTI otherwise known as critical limit threatening ischemia. LimFlow offers a minimally invasive technology designed to restore blood flow to the foot thereby preventing major amputation, resolving pain, and promoting wound healing. Prior to assuming the role of CEO at LimFlow in August of 2016 Dan had more than 16 years of leadership experience in the medical device and venture capital start-up arenas. Most recently, he was VP and General Manager of the EMEA Region for Direct Flow Medical. Here are a few of the topics we discuss in this interview with Dan:

- How LimFlow used concept that's been in existence since 1912 and then transformed it into a modern therapy that clinicians can reproduce.
- How the incubator MedStar played an instrumental role in the launch and ultimate success of LimFlow.
- Why it's essential to find a physician champion willing to invest time and energy into your technology.
- Overcoming the regulatory challenges presented by an ever-evolving MDR landscape.
- Reasons that convinced Dan to assume his first-ever CEO role at LimFlow.
- The importance of ongoing R&D and innovation to a company's success and sustained relevance.
- Why the FDA Breakthrough Devices program has been a game-changer here in the US.
- The importance of having a mentor.
- Why Dan would not give advice to his 30-year-old self.

Let's get to the interview with Dan.

All right, Dan, welcome to the program. Really appreciate your coming on, especially considering it's late on a Friday evening your time.

**Dan Rose:** It's a pleasure. Thank you for having me

**Scott Nelson:** Norbert's you're in your captain's chair I imagine there in Phoenix. Are you ready to rock?

**Norbert Juist:** I am ready to go

**Scott Nelson:** As the listeners know I provided an intro to your very impressive background, but to help contextualize everyone for what you're doing now with LimFlow can you give us an idea of the technology, the product and maybe just walk us through who a typical patient is and what LimFlows technology is helping to solve for

**Dan Rose:** Sure, sure, absolutely. LimFlow is working in the peripheral vascular space and so outside the heart but in the vasculature and primarily is focused on critical ischemia what everybody's calling now chronic limb-threatening ischemia. So, CLTI rather than CLI but essentially you're dealing with patients who have compromised arterial vasculature either from arterial sclerosis and also from long term experience of diabetes and are really at risk of losing their limbs. LimFlow is focused not only on these difficult end-stage patients but truly on the end of the end-stage patient. I think the best analogy for this is if we think about where tabby started or tavern and working with the extreme risk patient population where you know surgery was off-limits and the same is true for our patients. We're specifically focusing on a population of patients who have what we term no options, so they have no further endovascular or surgical bypass possibility.

So, they're essentially being consigned to major lower limb amputation, which is one of the scourges of the modern era. I mean, there are so many patients out there in roughly 125,000 major lower-limb amputations in the US. It's becoming a bigger and bigger problem because patients, of course, are living longer with their diabetes cardiovascular disease, and the prevalence is going up with both as well. If you survive long enough the arteries in your legs are not going to be able to provide enough blood flow to your feet. If you have diabetes developing an ulcer is quite easy to do and you'll end up with an ulcer, a wound on your foot that can't be healed. So, we're trying to keep those patients from getting a motor major limb amputation, and the morbidity to mortality is extraordinary. I mean, it's listed in New England Journal of Medicine published Major limb amputation is the fifth or in the top five most dangerous surgical procedures in the US.

Average morbidity, mortality depending a little bit on above the knee or below the knee, but is roughly 10% in hospital following major lower limb amputation. So, something to be avoided? Absolutely, and mortality is very high in the first year even if you do get out of the hospital. So, what we're doing is what a LimFlow patient is, is a patient who is faced with really, all of our patients so far treated are indicated for amputation. What we're trying to do is use the Venus system as a pathway to reperfuse the patients. So, if you think about the arterial system and arterial sclerosis. I mean, you have a lot of calcium and plaque blocking the arteries down into the foot and the best analogy is to think about driving to the airport and you get stuck in traffic and, Waze starts to tell you you're going to get there tomorrow and not today. You look across the median and you realize that that road, the other side of the road, goes where you want to go. It may not allow you to drive as fast as you want to go. It may not be ideal, but it certainly goes to the airport, and that's what we're doing.

So, we're creating a connection between the artery and the vein in the lower leg and then knocking out the valves in the veins going down to the foot and in the foot and then using covered stents to channel blood from the arterial side and the tibial arteries into the veins and driving it down into the distal pedal area and then healing wounds, which is the real goal because if you can heal a wound, you can normally keep the leg on. So, that's the concept. It's a concept that has been around, first surgically reported in 1912 but with a lot of morbidity and mortality. What we've done is essentially take the principle of that and turn it into a purely percutaneous

reproducible, co-morbidity, teachable, adoptable therapy that can be deployed whether they are interventional radiologists, vascular surgeons, interventional cardiologists, etiologists, anyone working in the lower leg can do this procedure. So, that's what we're trying to do.

**Scott Nelson:** It's super fascinating. I think that helps create a little bit of context for the rest of the conversation because really curious to learn a little bit more about what attracted you to LimFlow, especially considering your experience, but also how you think about the early stages of bringing this technology to life. But before we go there let's talk a little bit more about the technology. You said. It's been around since the early 20th century. This stuff always fascinates me because it's like, why are we not seeing this until today? So, can you help us? Kind of go back in time a little bit and understand how this concept went from something that was seen in textbooks to like applying actual percutaneous techniques and making this somewhat of a reality.

**Dan Rose:** Yeah, so what had happened is that this has occurred in many different areas of medicine. So, someone proved the principle in a dog in fact. Then people have done small surgical theories, a vascular surgeon here, a vascular surgeon there as kind of a bailout, trying to save legs at the last step, really, after patients of failed multiple interventions. But no one had ever really taken a look at one, how to do it for percutaneously continuously but two, really look at it in a structure of methodical way.

They're a bunch of reasons why it's very difficult to do surgically and one big reason, which is that you create a large surgical wound. When you create a large surgical wound in a patient that already has trouble healing wounds, you tend to lose the leg because of the surgical room. So, there are a lot of reasons why it has not been done percutaneously but ultimately what happened was that a very well-known cardiologist Martin Rothman from the UK, who ultimately became the Chief Medical Officer for Medtronic Vascular and who has always been an entrepreneur noted that people were trying this in the cardiac setting, and some patients were doing very well but some patients were not.

Obviously, if you fail in the cardiac setting, the price of failure is very high. But he thought, Well, maybe this is something that we can do and prove out in the leg. Being a super busy guy, he went to an incubator called MD Start in Europe, which was founded by Medtronic and Providian and Sorin and Sofinnova Ventures and Versant Ventures as a kind of way to take physician ideas and ultimately take them and incubate them if they looked promising. So, so that's where the experience and history came together to try and start this percutaneous approach. Acquired some IP from the old trans vascular business. It was acquired by Medtronic and founded by Josh Makower NEA and started to build prototypes and a business around that. Partner at MD Start Tim Lenihan who is an incredible guy. He really took the lead on founding the business in 2012 and I joined in 2016. So, there was a four year period where they were developing prototypes and doing first-in-man in Singapore before ultimately moving into the CE Marking phase.

**Norbert Juist:** When I was with Cordis we had that OUTBACK Re-Entry Catheter and that's kind of what this reminds me of, that I could just picture this doctor who's almost like a mechanical engineer in their mind trying to re-invent a better way to do this. They probably saw the re-entry

catheters that are out there and tried to come up with a better way to try and save these patients' lives.

**Dan Rose:** Well, that's exactly what happened. So, when they were trying to do the first procedures they really were taking technology that was off the shelf and starting the work and then realizing as they went forward what technologies need to develop internally to optimize the procedure to perfect it and there are several pieces of it that were not available off the show. So, what LimFlow is today is kind of a suite of technologies. It's an ultrasound-based crossing system with a needle on an arterial stent catheter if you think about it that way from Ultrasound and a Venous receive catheter. It's a Valvulotome or reverse or Push Valvulotome that allows us to in a very elegant way knock out the valve in the veins and then a conical covered stent so that we can match the diameter of the artery with the diameter of the vein and then our own covered stent platform that allows us to really channel the blood from the crossing all the way down to the foot. We have a bunch of other further innovations in progress. So, it's been an experience of doing exactly that, taking what's there and learning as you go. I think that's something that anyone who has been involved in early innovation in the med-tech space can really understand.

**Scott Nelson:** And in terms of a timeline, Dan, can you help us understand that a little bit more? I know you joined in 2016. When did Dr. Rothman first bring this concept to MD Start?

**Dan Rose:** I think it was around 2011.

**Scott Nelson:** Okay.

**Dan Rose:** And then they founded the company 2012 and they did first-in-man in Singapore through basically being introduced to a vascular surgeon named Steven Kume, who was very interested in the space and willing to take on the kind of project from a medical clinical point of view of just, you always have to find that physician who's willing to invest their energies and passion into figuring out something like this and go through the ups and downs. So, there was a series of patients. I think it was seven patients done in the first-in-man series in Singapore and that really proved the concept, led the raising of Series A and the doing of a small CE Marking study.

On the back of that being able to raise Series B and really take the company and hire a full-time CEO which was me because Tim was working on several projects at the same time. So, MD Start is a fantastic concept because what you end up with is a start-up that has been incubated by a person, a CEO with a tremendous amount of passion, but also with a tremendous amount of knowledge about how to do it well. A lot of first time CEOs don't know how to put together An IP portfolio. They don't know how to put together a regulatory strategy. They don't know how to do a lot of the different work that needs to be done to really create a strong foundation for a growth company because they're doing it for the first time. If you have somebody that is doing it for their sixth or seventh time and has had tremendous success doing it, then I think you're going to end up with a higher likelihood of success over the long term.

**Scott Nelson:** Got it? So... Oh, go ahead Norbert.

**Norbert Juist:** I was just going to say what determines then, with MD Start. Dr. Rothman's a British physician. What makes them decide whether you guys start-up in Europe or go for the CE Mark or whether you come to the US and go for FDA approval?

**Dan Rose:** Well, I mean, that's a great question because it touches on some of the dynamics that have changed over time. I mean, with MDR and a lot of other things that have happened in the space ultimately. MD Start was based in Switzerland back then. I think Mark Rothman was living in the US. Tim Lenihan was based in the Czech Republic, but they ultimately founded the company in Germany and did a lot of the engineering work with Contract Medical International, Bayer, and had the IP there and this tremendous amount of medical engineering consultancy talent in Germany and sub-suppliers. So, ultimately it was set there because MD Start was European based and at that, I think the CE Mark process, certainly it was a whole lot easier and more predictable than it is today. I hope I don't have spent too much time talking about MDR because I'll just get more and more upset as we go.

Then that was the real milestone that a start-up could aim for, getting CE Marks, generating some value in the company, generating on the back of that CE Mark further funding which is the lifeblood of the start-up. So, that was how they structured it. I think people now are looking much more to the EFS, early feasibility program in the US which we've completed with 32 patients. EFS, pretty familiar with how that works as a pathway than going through the old CE marking. But we're a European company, we're based in Paris and about half of our employees now are in Europe and then half for LimFlow were actually in the US. Our leadership team is actually split between Europe and the US. So, we're a truly international organization.

**Scott Nelson:** There are two things that really stand out listening to your answer there Dan and I don't want to spend too much on MDR but I would like to spend a little bit of time, so I don't want to go too into the weeds because it's something that we're dealing with, with Joovv the company that I'm involved with. It's a start-up that I'm involved with and trying to navigate those waters can get really complex, really quick and it almost seems really unnecessarily complex. So, can you just speak to maybe what the challenges are with MDR really within the context of what other med-tech entrepreneurs should be thinking about?

**Dan Rose:** Yeah. I mean, I think MDR means a lot of different things to a lot of different people and groups. I mean, if you're a class one device, I mean you may be asked to generate clinical data on things that it's very difficult to generate clinical data on. It's difficult to do a clinical trial on the scalp. Some of the things that are being asked to recertify are just difficult practically to do especially when you have hundreds of different products. It's not incredibly difficult for us at LimFlow because we are generating a lot of clinical data. We're already a class three system and so a lot of what MDR is requiring is not necessarily things, and we're already active with the FDA. So, for us, it's an inconvenience because it's causing systemic disruption with the notified bodies.

You can't get things pushed through because they're so busy trying to figure out the MDR and they're not sure what exactly the requirements are. So, the whole system is kind of overwhelmed, as it were. So, as a start-up, you have to really try and understand. Can you understand and determine well in advance what the notified body is going to want from you to get approval? I'm

not sure they can clearly tell you today if you came in fresh. Two, are you going to be able to get their attention, or will they even take you as a client today, which is another challenge, and then three, what is your timeline going to be? Because our timelines that I won't share who are notified body is or what the timelines are but they're very long and very unpredictable.

If for example, you CE Mark as a milestone for funding, well, how do you know how much funding you need? It could be six months for a response or 18 months for a response. So, I think it's become really challenging to have a predictable system and it's created, I think, just a higher bar overall which in some ways isn't a bad thing but in other ways is making Europe less attractive is a place to start. I do think that some people are certainly either choosing to go to the US first or staying in the US and even looking at the US and China or China first. It's very easy for Europe to become the third or fourth place you go for regulatory approval rather than the first. As an American that's lived in Europe for 20 years, I'm a big promoter of the European system. I mean, this is where I've spent a lot of my professional career, and it's disappointing to see the shift happen.

**Scott Nelson:** Yeah, it's really interesting because that used to be such a trend is to commercialize in Europe first, primarily from a regulatory standpoint, because FDA was maybe more onerous from a timeline perspective. But it seems like those winds are changing.

**Dan Rose:** They are, and it will be some time before with the best will in the world and I think the parties are trying to do their best but it's a real challenge, we can say that.

**Scott Nelson:** Got it. The other thing that is interesting and I don't think we may necessarily need to talk a lot about it. But I was unaware that there's a strong med-tech ecosystem in Germany. I know specific to what we're doing at Joovv as an example it's amazing to see what's happening. The things that are happening in Malaysia and how many other companies are pulling out Shenzhen as an example. But Germany, I didn't know that was a hotbed for med-tech.

**Dan Rose:** Sure, there's always been a strong med-tech presence in Germany. I mean, think about Biotronik, you don't hear about it much in the US, but it is a massive multi-billion dollar family-owned but huge presence and a lot of engineering talent out of there. The ABBYY emit technology came out of Germany. Go down the list. If you include Switzerland in there then you've got Symetis, you've got [21:32inaudible]. I mean, there's just a list after Ypsomed acquired by CryoLife recently. I mean, just story after story after story of a large med-tech presence in Germany.

Remember Germany, in Europe is the place you commercialize first if you can get reimbursement. [21:52 inaudible] was very much driven by Germany and that drove the whole global expansion of that therapy. Because being able to see how quickly and explosively this could be adopted by the community meant that you could invest in the space and you could drive towards US approval and have data from Germany to do so. It's a great place to be. We're now in the French ecosystem, which is also a good and ecosystem, but not truly comparable to the Silicon Valley or Minneapolis. I mean, those are different in order of magnitude, different in terms of what's going on.

**Scott Nelson:** Sure, Norbert, if you don't have anything else to add, I'd like use this as a transition point to talk a little bit of more about Dan what drew you to LimFlow and how you began to think about taking the technology and commercializing it whether it's in Europe or maybe future plans of commercializing in the US as well. But I know we'll get to this later on in the discussion about maybe some of the learnings you took away from your experience at Direct Flow. But what was the appeal to LimFlow back in 2015/2016 when you joined the team as the CEO?

**Dan Rose:** I had known Tim Lenihan for some time and he'd actually talked to me about LimFlow a couple of years before I actually took this job. But I was very clear. I'm like that's not really my stage. The early prototype stage and first-in-man. I've been involved with it, but I was really looking forward to the time when the technology could be somewhat de-risked because you're a CEO and taking on any start-up job you're really investing yourself completely in the technology but I had looked at it and tracked it and I could see the potential. A lot of what we do in med-tech, for better or for worse, is iterations or improvements on current technologies. A new flavor of a stent, and I've done that. I lead marketing for coronary vascular for Medtronic and the whole stent business, etc. That was gratifying. But I was looking for an opportunity where we could really deliver a transformative kind of value to space. The more I looked at the CLI or CLTI space, and the more I understood about LimFlow, the clearer it was that this was a tremendous opportunity.

Also, to do that, you only have to know that the only two categories of products approved to treat critical [24:21 inaudible] in the United States for the FDA are plain old balloon angioplasty and I think one single [24:26 indication]. So, this is one of the hardest [24:31 inaudible] sclerotic situations and cardiovascular situations to deal with and it's a nice to a gunfight. The opportunity to make a huge impact on that space is what drew me in. Also, LimFlow was a clean slate at that point. So, there were no employees. Everything was done by consultants. So, I was able to come into a well-funded situation. We'd just pulled him a 15 million Series B and build a team that was the right team that I wanted. As a first time CEO, they're a bunch of things that are critical. One of them is funding, and two of them are the right team setting and three is just the right technology. I felt like all three of those things were there because as a first time CEO. By definition, you don't always know what you're doing and the more factors you could put in your favor the better. But really, it was the opportunity to change and deliver the value of space. That's what motivates our whole team every day is the fact that we're taking these patients who are headed for a terrible, terrible medical outcome, and saving limbs is saving lives and that's what we're trying to do.

**Scott Nelson:** Got it. Certainly, it's pretty easy to understand the compelling nature of the technology and to do something truly disruptive to that segment of the patient population, for sure. But on that note, when you think about there's this whole other animal which is the business side of med-tech. So, when you walked into this situation, which sounds pretty appealing, the clean slate, well-funded, opportunity to build out your own team. What were your early thoughts about actually making this a real thing in Europe, really maybe more within the context of coverage and reimbursement? How do you actually get payers to pay for this technology?

**Dan Rose:** Well, I think it goes back to some of the issues we talked about before with CE Marks. I mean, we achieve CE Marks with a relatively small study, and we've done a lot of work in this space since I joined. But even though the health economics of LimFlow is just tremendous. You really can't ask for a better health economic value generative story because you're standing right next to an extremely expensive, extremely poor outcome for patients and if you can avoid that, which is what we do, you're going to deliver a lot of value for the technology you are providing. But ultimately you need a lot of data to prove that to a reimbursement authority. That's true for France. It's true for Germany. It's true everywhere. So, what we decided pretty early on is we're not going to commercialize in Europe now.

We're going to focus on building a global data set. Part of that's going to be done through an early feasibility study in the US and then a pivotal trial. Once we do that, then we're going to be able to come back and get the reimbursement we need to deliver the maximum amount for the company. So, we've done a bunch of different things that are different from maybe what start-ups too. But one of them was just saying, okay we may be in Europe, and it may be obvious to try and start commercializing, but it's a very expensive process. If you can't get formal reimbursement, you're going to be swimming upstream in a very difficult situation for the foreseeable future and probably wasting a lot of money that you could be spending on other things like generation for the clinical data and further R&D.

This is one thing I'd like to stress. I mean, if I have learned anything over my time in multiple start-ups is that you can never stop innovating. You can't think that you have solved the problem because as you go forward, you should be learning from all your experience. If you are in a competitive space and this harkens me back to a little bit what you alluded to, which was the Direct Flow medical experience. If you're in a space where you may have the right solution, an advantage over what others have today, including the strategics, everybody's innovating, and they will catch up. If you don't continue to keep your lead or advance your technology, ultimately you'll lose relevance. I think that's one of the things that we're doing it LimFlow. We are just about to launch our second-generation system.

The third-generation system is in development, we're deeply involved in IP generation and making sure that our knowledge and the experience we've gained is going to be value for the company, and it's going to be translated the better products for people. So, that's not easy because R&D costs a lot for a start-up. But I think if you've got the right board and you've got there is a strategy, you need to continue to do that because you have to be executing on your five-year plan, not your one year plan. The five-year plan has to be updated every year. So, I think those are different ways that we have thought about it.

Specifically of reimbursement though for the US we've benefited, and I wish I could claim responsibility for this, it had nothing to do with me. We achieved what was called back in the day the expedited access designation for the FDA which became the breakthrough technologies designation. The summer CMS Medicare in the US published guidance that indicated that breakthrough technologies would be eligible upon FDA approval if they met certain requirements. This is a tremendous advantage to the US system now is if you get a breakthrough

technology indication, you have a very high likelihood of having reimbursement when you launch in the US. I think that changes the game. I wish that were true in Europe but it's not. So, we're very focused on that, because we can now move forward with confidence that when we deliver the data we're going to deliver, we can immediately start delivering the device to the community that wants it.

**Scott Nelson:** On that note Dan could we spend a little bit of time talking about that breakthrough technology. In your experience what is, and I know you're not a regulatory expert, per se, but I have a feeling you know enough to be pretty dangerous there. What's the likelihood of a technology being accepted into that program with the FDA?

**Dan Rose:** Well, we've seen a raft of them. If you track it, it seems like one every week has been getting. I think Celmatix got one just a couple of days ago. Ultimately, you have to be focused on an area clear unmet need for the US Healthcare system or population. So, it's obvious when you look at us. We're serving a no option patient population that is causing a massive healthcare expense and massive healthcare crisis. So, patients can't be treated any other way by definition, according to our protocols. So, we are a breakthrough solution, and I think the very wise view of the authorities in the US has been well, okay, if this is truly a breakthrough solution, we need to make sure that there's this interim reimbursement so that people could actually use this when it's available. I think you have to look closely at the program, but this is a game-changer.

There's always been talking about this valley of death in the US where you know you get approval, but you can't really sell because you're waiting for [31:38 inaudible] but you don't get [31:39 inaudible] and this really does change the game. I'd like to just mention one other warning because you asked about it, which is something that a lot of start-ups don't do, and I didn't do in one start-up where I really wish I had. But in LimFlow we did it, which is we spent a fair amount of money on market research and I think if you're doing something that is new and is in a space that is relatively unstudied. I think there are a lot of medical areas that are relatively unstudied in terms of market research. If they're selling stents into it, if they're selling hips into it, obviously they're going to be great market reports. But if you want to find out how many no option patients there are, very difficult to do.

Back in the day with TAVR if you wanted to find out how many extreme risk patients there were very difficult to do because nobody treated them, nobody referred them, and nobody treated them. So, we invested in the large independent market research and we found out that there are just a ton of them out there and we can prove it. I think that allows us one to raise money because people can really say okay when you get there, there's going to be a market for you and it's going to be a big market and it's going to be your market and. I think if I raise money once without the market data and then got the market data and it's just so clear if you've got it in your hand and it's independent, you can answer one of the questions that's quite difficult to answer sometimes for people doing...

**Norbert Juist:** So, on the business side of things one of the things that I wonder if you talked on the mortality rate of things that I know that the five-year mortality rates in these patients, is horrendous. This is a product that I think I read somewhere, maybe on your US part of your

website, that there are 270,000 patients. Give somebody who's driving in their car listening to this podcast right now some perspective. Is 270,000, is that just the US. Is there a business here for a standalone company or is this something that you know would sit well in an atherectomy company portfolio? Because once they've tried atherectomy, Medtronic tries that, and it doesn't work. Now they've got something else to save this patient's life essentially.

**Dan Rose:** Yeah. I think there are a couple of questions in there. One is as a standalone company we're talking about in just the no option patient population about 88,000 essential procedures a year only in the US. About 350 globally and major markets. You're talking about a $1.3 billion opportunity in the US alone, and so can it be an independent company? Absolutely. I mean it is a huge opportunity, and we are positioned to, unlike the other parts of peripheral vascular where you're competing with somebody else's stent or somebody else's balloon or somebody else's catheter. This is a LimFlow market, and so we anticipate a true ability to build a franchise here.

Now our technology is a technology that is well understood by any sales rep, a clinical specialist in the space. Therefore, would it be a fit for any number of major strategic salesforces? Absoluto. I think it is an insight into the business. That's how we're thinking about it today. We're driving to that, but ultimately can it be part of the bag of another company? Absolutely. I think the more we're out there, the more that LimFlow has talked about, and when I started people were telling me no option patients don't exist. Now you go to any major peripheral conference. There are separate sessions on DVA, [35:21 inaudible] not sponsored by us. This is becoming part of the lexicon of how people understand how to treat these patients. It will only increase as we go forward. Just next week, we're in the late-breaking trial at Viva. You'll see more data. This is the beginning of a big, big story.

**Scott Nelson:** And Dan I want to circle back around to something you said earlier it with respect to market research because it's sort of ties into your answer there in terms of trying to define the traditional TAMS and SAMS. I think that's super interesting that you call that out because I wouldn't have expected you to mention that. So, in essence, if I'm understanding you correctly, you're saying, don't simply rely on off the shelf reports in some instances. Allocate the necessary funds to go study a market independently to determine real actual numbers. Because that may not only confirm kind of your suspicions about a market size but also be a really good data point in terms of raising funding too which is obviously needed for any med-tech start-up.

**Dan Rose:** I mean, the easiest way to break it down is to ask the board. Should we spend 30 million, 50 million, 20 million euros to develop a product for a market that we don't understand very well? And the answer is obvious.

**Scott Nelson:** Yes.

**Dan Rose:** You just spend a couple hundred thousand dollars, $100,000. We're an engineering-led space, and that's the engineering medical, that's absolutely right. But ultimately, you really better understand if there's going to be someone there to buy your product and what the dynamics are before you blow a ton of money going down the wrong way, not understanding the needs of the market and understanding how many people are really out there for it. So, I think

money is precious for every start-up. If you're not doing this work, I think if you're in a space where it's ill-understood and there are those spaces where it's ill-understood, then you do have to go out there and do the work yourself.

Don't try and triangulate yourself. I think the VCs see right through it. But you can say, look, here's an independent. We have 51-hour interviews with experts in this space that we didn't do, and they're not only telling us that our market is bigger than we thought it is, but they're telling us they're all these other applications for a technology that we didn't think about. Imagine what kind of response you get and how much easier it is to proceed on almost every level with the confidence that if you get there, there's going to be someone who wants to buy what you're selling. Again, it's a takeaway. I didn't do it at the beginning, but I would not do it again.

**Scott Nelson:** Got it. Yeah, super interesting, that's something that really stands out. The key takeaway there for myself. I know for sure, and I'm sure for other listeners as well. I want to be cognizant of time here, Dan. But one other follow question to something you mentioned earlier about clinical studies and really doubling down on the collection of clinical data. Is there anything that stands out or that would be good for others to learn from in terms of your approach to where you're doing and where you're sponsoring and enrolling studies. I know you mentioned Singapore was sort of the launching pad largely because you had an engaged physician there. Outside of that, within your approach to when and where you're starting these clinical studies.

**Dan Rose:** Yeah. I mean, you have a lot of discussions with other CEOs about this because people are always trying to figure out what the fastest way and what the best regulatory place to do it where you can collect good data. It depends a little bit on whether you need long term data or acute data. All of these are big factors. I think a couple of things that I would just say are critical more than where you do it. That is excellence in what you do both in pre-clinical and in first-in-man in terms of data collection, in terms of structure. You're going to live with that data for a long time. I mean, the FDA is going to want to see everything you ever did ultimately. If you're successful and you have to think about that. If we are successful, ultimately this is going to be part of our path. So, do it right if you can and if you have the right money. Try and do it right.

Doing it fast is great but just remember somebody's going to look at that later on, and you need to be cognizant of that from the very beginning. You've got to find a great advocate, a great position supporter, someone who is willing to invest the time to really learn with you. So, there are a lot of factors and basically, you have to get lucky in many ways, I think as well. But I think more important in place is just how you are thinking about what you're doing. A lot of times people are doing things quick and dirty. I'm not saying you can't do certain things that way. Just figure out what's working and what's not. But just remember everything kind of counts and if you do it poorly at the beginning or make some mistakes in your assumptions, it will catch up with you, that's for sure.

**Scott Nelson:** Good stuff, Norbert, If you're cool with kind of moving on, I'd love to kind of summarized maybe some of this discussion through a couple of questions in regards to your previous experiences Dan at both Direct Flow Medical as well as some time you spent at High Plains, which is a boutique venture capital firm, Thinking about those experiences there. I know

you've kind of covered a few of the kind of key learning points or things that you do differently. But is there like one or two other things or pieces of advice that you've learned from in those experiences that you'd offer up to other med-tech entrepreneurs or people that are better at med-tech start-ups?

**Dan Rose:** I think there are a few things, I mentioned some of them. One is about just never stopping R&D. I think I think that's continuing to innovate. Startups do innovation so well, in a way, the big companies can't do it. These are advantages in a way right. We're nimble and we can learn, and we can move fast. So, keep doing it right and be responsive to what you see out there. Don't just believe you built this perfect little thing, and everybody should come and love it. I think there's never been a medical technology that couldn't be improved, and sometimes it's not your technology. Sometimes it's no-look, I don't need to keep harping on about TAVR but it's true for inflow certainly. A lot of the innovations and improvements and outcomes came from imaging for example.

Understanding how to prepare for a procedure, how to use imaging during a procedure for a lot of interventional things. These are key. So, it's not just about your technology, it's about the setting it's in and making sure that you're tracking that. I think the only other thing I would say is you've got to have a Plan B. Things go wrong. I mean, if there's one rule if things go wrong and it's usually things that you don't want to go wrong, go wrong. So, if you can have a fallback strategy, make sure your board knows that it can go wrong and knows that you have a fallback strategy. I think you should all be in the same boat together so don't fall in love with a single pathway. Have a Plan B and that saved me in a number of settings, and it seems like extra money, but we all buy insurance in our private lives. So, trying to understand that if you don't solve it that way, there is another way and you're already working on in the background. I think those are real takeaways. Hard-earned, painful...

**Scott Nelson:** Lessons learned by fire.

**Norbert Juist:** Well, and one thing that I have heard of companies that have done that midstream and what has prevented them from making maybe some new iterations or changes in the approval process that they have gotten their hands slapped because they made a change without then putting it back through FDA trials. So, I found that interesting when you had mentioned that you guys already were on your third iteration or improvement. I wondered do you have to then go back and resubmit and does that cost additional money to go through those trials again?

**Dan Rose:** Well, that's a great point because everything needs to be done in the context of the regulatory strategy. You need tremendous regulatory capability in-house. One thing I did at LimFlow, very early on we had a great consultant who helped us get the expedited access pathway and was doing a great job. But we're moving into starting an early feasibility study, and I said, look, this is great, but I cannot go around telling people that our main goal as a company is to get FDA approval and not have complete ownership of our regulatory interaction with authorities in our strategy. So, I invested in just fantastic... Zachary Woodson is an incredible regulatory guy, ex Medtronic, and Claret Medical and Conor, and just an amazing person, Difficult, expensive to have a full-time resource.

You know, you've got to do your R&D in the context of what can we change? What can we do without restarting or can we use this in this trial and then in the next trial, be ready to slot in the improvement? So, these are not easy things to navigate. So, I think investing in regulatory ownership of the process, I think, is key. I decided very early on the hire an American do that because I felt that I wouldn't hire an American to manage a French regulatory process. So, I figured I should have an American to run an American process and not a French person. So, I think culture also matters. I hope that doesn't create too many angry listeners out there. But I think culture does matter in some of these things as well with regulatory authorities. Until he made that investment and it's paying off because you can't consider R&D and cycles without really knowing what you can and can't do.

**Scott Nelson:** That's good stuff. So, I know we're short on time here. So, let's go ahead and get to the rapid-fire questions Dan if you're okay with that,

**Dan Rose:** Yeah, sure.

**Scott Nelson:** Sounds good. So, the first one what's your favorite business book?

**Dan Rose:** You did let me think about this beforehand, but the answer to me was so obvious right off the bat. It's not a business book, but I think I thought immediately about endurance. The story of the book, Arthur Lansing's book about Shackleton and going to the south trying to cross the South Pole. You want inspiration for being in a start-up, a medical device start-up. I think looking at someone who set out to do one thing and survived a lot of different unanticipated challenges in an amazing way. I look at that and say, this is an adventure we're on and we can't pretend to know what's going to happen. We can try, but life surprises you, and it's all about how you respond and how you carry forward. If you really pressed me, I have to go back to Bill George and "Authentic Leadership" and kind of Medtronic reference, but I haven't been at Medtronic for years. But yeah, Shackleton and Endurance, have to go with that.

**Scott Nelson:** All right, Cool. Still bleeding a little blue it sounds like. On that note, the second rapid-fire question is there a business leader or mentor that you most admire or one that stands out in your career?

**Dan Rose:** Well, I mean, now you've asked me to be slightly heretical because I'm a huge fan of Miles Lowell Edwards. I think this whole TAVR, how it's been developed, the whole story of how they manage comprehensively the innovation side, the clinical data generation side, the reimbursement side, the market development side, kind of a ferocious competitor on the commercial end. I mean it's a really, really cool story. I saw him speak in a very small group one time, and that's a story I think we can all look and say that was done right.

**Scott Nelson:** Yeah, There's no doubt every time I'm based here in Southern California and I drive by the Edwards HQ fairly, often, maybe like once a week or once every couple weeks, and I every time I look at those big buildings, it's always just impressive what they've been able to do with that space for sure. So, last rapid-fire question before we go and conclude the interview. What one thing would you tell your 30-year-old self?

**Dan Rose:** Well at some level I wouldn't want to spoil the story. But I would say I spent a lot of time, especially my days at big company worrying about politics and whether I was in or out or what was going to happen and many things that I didn't have any control over. I think I would have had many more hours of sleep and a lighter experience overall if I just realized that you can't sweat the politics,. You've got to just focus on building teams, working with people, getting things done, and let everything else just fix itself over time. It's a ride and it's going to be ups and downs, but it's been just fantastic. I'm really looking forward to seeing what's next.

**Scott Nelson:** Yeah, that's such good advice. It certainly resonates with me for sure. So, Norbert anything else to add before we go and wrap this up?

**Norbert Juist:** No, no, I just want to thank Dan for his time. That was really interesting, insightful stuff.

**Scott Nelson:** There's no doubt, Dan, Thanks a ton for your time. I always feel like in a conversation like this it's hard, almost to conclude it just because there are so many other things that we could dive deeper on but maybe we'll do a different version of a podcast at some point where we'll do the Tim Ferris three hour interviews.

**Dan Rose:** Maybe you can have me back one day and I'll tell the LimFlow story in full.

**Scott Nelson:** There we go, there we go. I always love the part two stories where we can kind of come back and look at what you guys accomplished.

**Dan Rose:** You can hold my feet to the fire.

**Scott Nelson:** That's right. That's right. If you want to go more and learn a little bit more about LimFlow I encourage you to go to the website LimFlow, l-i-m-f-l-o-w.com. I will include that in the show notes for this interview at medsider.com. Again, thanks everyone for listening in LimFlow's got it, Dan, and his story and what they're doing at LimFlow is very compelling and it will be really interesting to see what you guys accomplished. So, thanks everyone for listening until the next episode of Medsider Radio.