

Talks at GS

The pace of innovation in biotech: Mirador's Mark McKenna

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Mark McKenna: Inherently, we're going to take risk. We're probably going to take risk in ways that big pharma wouldn't.

Dan Dees: I'm delighted to be joined by Mark McKenna. Thank you for being here with us. Mark is the CEO and founder of Mirador Therapeutics, which is a company driving a new era in precision medicine, focused on autoimmune and inflammatory diseases and focused on moving with speed and accuracy.

And I'm rooting for every entrepreneur in the audience. I love all your businesses. I'm excited about all your businesses. I'm really, really, really rooting for you. Please keep making the changes you're making in medicine. Keep making the progress that you're making in medicine. It's so important and so valuable.

I first got to know Mark in his previous iteration. He was the CEO and chairman of Prometheus Biosciences, which we helped him sell last year. It was also a precision medicine business. We helped him sell it last year to Merck for \$11 billion. And so he knows of what he speaks. He's got an incredible track record of success and I think has a lot of wisdom and advice to share with an entrepreneurial crowd. And before that, you had decades in large-cap pharma and a variety of other health care businesses over a decade.

So let's dive in. And maybe let's start with that. What advice can you give to a group of entrepreneurs? And what did you learn as an entrepreneur from those decades you spent in large companies and in large-cap pharma specifically?

Mark McKenna: Yeah. First and foremost, thank you to Goldman Sachs for putting on this event and, Dan, for offering this opportunity. Really enjoy getting to know many of you here and am inspired by the work that you guys do.

You're right. The stakes are high in what we're doing.

There's many biotech entrepreneurs here, and earlier David spoke about the fact it's about doing good and reciprocating on the other side. And I really feel like what we're doing is a pretty noble profession. And the second time around where money isn't even a consideration, it's more about how do we move the field forward? How do we improve patients' lives through our products?

Look, to answer the question around what were the learnings that you took from big pharma, big health care into biotech? Let's make sure we orient the audience in terms of, like, the ecosystem. So for the past 100 years or more, you've had a handful of big pharma companies that have driven most of the innovation in the space. You think of companies like Merck, right? 200 years old. J&J. You can pretty much count those on two hands. So that's what you had until basically 1980 when all of a sudden you had the emergence of a number of new groups like Amgen, Genentech, Regeneron. Familiar names, right? Hard to believe it's, like, Amgen has, like, 200,000 people now. It started as a little biotech company in Thousand Oaks. And so I think it's important to have the orientation there on the ecosystem.

Big pharma is really good at developing process, commercializing drugs. Sometimes they're good at capital allocation. I use the word "sometimes." But I think that they're too slow. And they realize this. And they're not willing to take as much risk as needs to happen in order to move the field forward.

And so what you saw with Genentech, Amgen, and Regeneron, is people that have worked in large pharma and said, "You know what? We think we can do it a little bit better, a little bit faster, take a little bit more risk." And those groups have kind of pioneered a path forward for us innovators in health care. Because what we do requires billions of dollars of capital.

So for example, at my last company, we raised both privately and publicly over a billion dollars thanks to the help of Goldman. And that only got us until basically through Phase 2 when we sold the company. A billion dollars. But I think it's really important that folks understand that like, we talk about this cancer moonshot. This ecosystem today is perfectly delivered to set up on that and in a way that it wasn't 20 years ago. Why? Because now there's 700 public biotech companies of which 80% of

them are developing drugs in cancer.

So instead of having ten companies all risk averse, they're pushing the envelope on what's possible. For me, biotech, it is the ultimate area for entrepreneurs in health care. To be able to take an idea and move it forward. It doesn't mean we're the best at commercializing drugs. Quite honestly, most biotechs shouldn't commercialize drugs, given the cost and the challenges and the expertise that are needed to do that.

So hopefully that orients everyone in terms of the ecosystem and in how we can potentially win. In terms of the learnings from big pharma to biotech, I think the biggest thing was something I learned playing team sports. It's how to lead organizations, how to deal with conflict, right? Each of you in your own businesses is people leadership not one of the most challenging things that you have to deal with day in, day out?

You know, I love the puzzles of the science. You got to be able to be a steady hand and know how to deal with people. And I think in biotech a lot of times you have these cowboys that come over from pharma. They can't work

with anyone, but they're brilliant. And being able to harness that brilliance and turn it into a product I think is kind of the secret sauce.

Dan Dees: Yeah, makes sense. And let's go back to your entrepreneurial journey a little bit. You know, my intro, I jump right to the success and you sell something for \$11 billion and you're off to a hot start with Mirador. What were some of the hardest times for you as an entrepreneur and as a founder?

Mark McKenna: Yeah. So maybe as a backdrop, so I was running a company called Salix Pharmaceuticals. It was a \$2.5 billion revenue stage company, mostly focused on commercializing drugs versus developing them. I got a phone call from a guy named Tachi Yamada, who's no longer with us. But Tachi was the past president of the Bill & Melinda Gates Foundation, former head of R&D at GSK and Takeda.

He called me and he said, "Look, we've got this platform idea coming out of Cedar Sinai to bring precision medicine to immunology, and we'd like for you to come run it." And I said, "You know, what stage are the programs in?" He

goes, "Yeah, they're all pre-clinical." That means that there's no -- like, there's no drug, right? It was more like, "Hey, we have pathway that we think, you know, if we inhibit we can actually stop some of the downstream inflammation and fibrosis in the body. You wanna go check it out?"

And I go, "Well, it sounds like a great idea. Maybe something I'd like to invest in. But it sounds like you need a chief scientific officer, not a CEO at this point." And my background came more on the business side than on the science side. I've obviously had to learn that to be able to articulate to investors and to our team how to make decisions. But the real thing here was I took a chance, after kicking tires, in my heart of hearts I believed where medicine needed to go was more personalized.

And we saw it play out in oncology where you started to identify single variants and develop drugs against those. Like HER2 in breast cancer. And you could see dramatic improvements in terms of overall survival rates like we'd never seen before. And I believe that that same approach of identifying certain subsets of patients could lead to improvements in efficacy.

We were developing drugs, in this case of this platform, it came out of Cedar Sinai. It was focused on inflammatory bowel disease and some adjacencies. Inflammatory bowel disease is about 5 million patients in the world, about 2.5 million in the US. And it's a chronic debilitating disease. You know, imagine you're 12 years old, you're a female, you're having to go to school. Like, you know where every bathroom is on the way home from school. And the same thing goes if you're an adult.

And so to me, it's like we had this admission around that we were the best hope to bring new therapies to patients in this area, and we had the expertise, the world's leading KOL that was part of the company, who helped discover some of the science. This was his life mission.

And so the question was around how'd you get kicked in the teeth along the way? And I'm surprised -- you know, these are mostly dentures that you see here because there were plenty of those experiences. Case in point, when I got there, I was told that the company had 18 months of capital. Well, what do you know? When you get there, things are a little bit different than what was pitched.

So literally day one on the job, my first thing I was doing was raising capital. We were still, like, fixing the plane as we were flying it, trying to figure out how we were going to make this sustainable. And again, the cost of entry here is really high when you think about to run a clinical trial and to get proof of concept, you know, you're talking \$30 to 50 million right out of the gate.

It took me 12 months to raise the first round of capital. I used to go home at night and my wife would be like, "How do you stay, like, engaged and positive?" because no one tells you no and everyone's telling you no. And we went into COVID. We had to restructure the business. In terms of the orientation, it was a mixed business model with diagnostics and therapeutics. We're spending 99% of our time on the diagnostic side, where all the value for patients and for the investors was on the therapeutics side. So I had to go back to the board and say, "Hey, you know, we need to change the configuration here."

We did a partnership with a group in Europe. I flew over to Europe using my United Airlines points. True story. And we got that deal done. We raised \$20 million in capital. It

proved to investors that a first-time CEO could go out and execute. So you cleaned up the business. You restructured it. You raised some additional capital through partnership. Okay, we'll take a bet on you.

And so we raised, you know, 12 months later, raised \$130 million, which was enough to fund the lead drug basically through mid part of Phase 2. And the first two years were super hard. The last two years -- it was a four-year run, the whole thing -- but the last two years was an unbelievable experience and partly why I'm back at it because I felt like I saw first hand the impact that our science was having on patients. Seeing remission rates go from 10% remission in inflammatory bowel disease to 25%, that may not sound like a lot but just from a business point of view, I think you guys get the patient impact here. From a business point of view, each share point's worth about \$300 million. So it's meaningful.

And imagine if you're that 12-year-old girl who has been rotating on Humira, Stelara, and all these other therapies, to finally bring something that was personalized for her that can get a much better outcome. And so those are some of the hard knocks of running a business and a

biotech.

You know, it is legalized gambling in some cases because it is so risky. Taking a drug from Phase 1 to commercialization, it's like 5% success rate. And so we feel very fortunate with the outcome that we had and, more importantly, the impact that we're having on patients.

Dan Dees: Yeah, it's fascinating. The science of it is so complicated and, you know, just so high risk, but there's also the business element of it. And we heard yesterday from Ryan Smith, who talked about the value of networks and building your network and having that benefit your business over time, maybe over a very long period of time. You've been a private CEO. Then you were a public CEO. Now you're back to a private CEO again. But you've been really intentional about building your external networks, both the corporate leaders and with investors. Talk a little bit about that strategy and how it's benefited you over time.

Mark McKenna: Yeah. A lot of what Ryan said yesterday resonated quite well with me and I'm sure with you guys as well. Look, you've got to be intentional as you build out because when I think about how did we get to an \$11

billion outcome, we went from no one taking my call to four Gulfstream jets sitting in the San Diego airport all waiting to take me to dinner.

Dan Dees: The second one was more fun, right?

Mark McKenna: What changed? And I think that that experience, first of all, we weren't developing something to be sold. We were focused on inputs, not outputs. And when we did that, we executed, we developed a great strategy, we built these relationships with investors that they trusted us. They knew that when we were setting out to do something, we were going to deliver on it. And we weren't going to embellish. We weren't going to hide the ball. We were just going to be transparent.

Which is why, when we went to launch Mirador, we raised \$400 million in, like, two days. It took me a year to raise \$130 million before. So if you want to just calculate the value of these relationships, there's your quotient right there.

And on the strategic side, maybe just an anecdote there that would be helpful for the other biotech folks that are in

the room. So we had to post our Phase 2 results. We had a number of pharma companies kicking tires, asking questions. And I remember calling Dan's team and saying, "You know, how do we coalesce this to figure out who's real and who's not?" And they said, "Hey, here's a case study of another company that went through this process of thinking about partnering the drug and doing, like, a joint development, joint commercialization type of approach." I was, like, yeah, you know, let's figure out who's real. And oftentimes in most of these transactions, it starts with a partnership conversation and then leads to an M&A transaction.

So we had really good counsel that gave us a case study that was rooted in data that said, "Hey, like, you follow this playbook, here's likely what's going to happen." So we got 17 groups under CDA. By the way, 86% of deals in this space are done with one buyer, only one bid, right? So we were putting out the vibe, making sure that -- in not a sales-y way. Like, we were confident in our own path. But hey, if you want to take a look at what we're doing, we're happy to do that. But just so you're clear, like, we're talking to others as well.

And so we went through this process. The data came out. And we set expectations from investors that remission rates would be around 10-15%. We got in at 25%. The biomarker, which is the way to stratify the patients, came in at 35%. The market went nuts. And I called up every one of those CEOs on Saturday and said, "Hey, we're not partnering this drug. Thank you for your interest but there's not a number you could put on the table right now from a partnership perspective that our board could accept and that would be viable for you as well. Let's stay in touch. Let's stay friends."

You know, I was at a couple different events with the CEOs of most of these companies, a networking event. And that's when Merck said, "Hey, we want to pursue this further. You know, you don't need to talk to those other companies. We want to buy your company." And I picked up my phone at dinner there and said, "Is there something in my inbox that I need to know about?" because he was talking so confidentially, like, "We're going to buy your company."

And again, we played this out for several weeks. And a number of other suitors were around the table, you know, trying to figure out, like, what is their angle to win. At the

end of the day, you have to have a realization as an entrepreneur that there's a time to hold and a time to sell. This is your baby. Am I really the best person to commercialize this drug for patients? And there's no way I could look myself in the eye or my family and say, "Hey, yeah, I want to see this all the way through."

And then the financial side, the impact that it had on my team. Out of 120 people, 110 became millionaires. And we saw people being able to afford to send their kids to college, to do all kinds of things that pay off debt and stuff like that that was life changing. And so I think that that experience and working with building these relationships really enabled a competitive process.

Dan Dees: It's so rewarding because all of those people took enormous risk alongside you. Both the investors but equally the employees because these things can also not work. And to have that outcome is just awesome. What a great thing.

Mark McKenna: Yeah, no, it is. I think it's really important that you structure your boards with people that can really give you honest and transparent feedback on

what you're doing right and what you're doing wrong. And I think it's too easy as entrepreneurs to put in people that are going to be yes people on your board. But are they really pushing and making you and the team better?

And the same goes for the partners that you put around the table. You know, are they bringing value? Are they telling you what's best for them or what's best for you? And that goes for M&A advisors. Am I really taking the best bid? And that's where Goldman I think really, in my mind, yes, they helped us tremendously with the financing but having the right M&A advisor to make sure that you're thinking about it appropriately, you got the right tension in the negotiation process, that was super helpful.

Dan Dees: Let me link the last session with this session, the political session with this session. Drug costs. You've been pretty vocal about this topic. It's obviously a topic that plays out in the political arena. How do you balance -- you've been in the guts of it, you've seen the cost of these things -- the value of keeping R&D in the US, the importance of innovation, and yet the need to keep drug costs under control? Give a perspective on that.

Mark McKenna: How much time do we have? I guess we have 7 minutes and 15 seconds, so let me do my best there. Let me attack two different topics. Drug cost, it's multidimensional, right, what drives it. We talk about the costs to develop these drugs. Those are real. But there is two major things standing in the way, in my mind, of drug pricing going down. Number one, it is the PBMs, pharmacy benefit managers, okay?

Somehow, some way, our government allowed the PBMs, the health plans, and the pharmacies all to vertically integrate. Don't ask me how that was allowed to happen. So let's say you charge 50 grand for a drug. Do you realize that about half of that, 25,000, goes back to the insurance company, okay? If you just look at the trickle down of the economics on drug pricing, you'll soon realize that the you have all these other costs. Co-pay, card buy downs and everything. It's a mess.

But the fundamental factor here in my mind that's broken is the PBMs are a middleman, and they bring little value in terms of innovation. I want every dollar in the health care system to go to find new cures. How about you guys? Right? So I think we need to solve that.

And the other thing that is standing in the way of lower drug pricing is employers. So one of the things that I'm grappling with with this new company is first-dollar insurance. So for those that aren't familiar with that, everyone knows that what's happened in the last 15 years is, because health care costs, not just drug pricing, but health care costs have gone up dramatically. Hospitals. Doctors. Surgeries. Drug cost is a sliver of that, right? But it's an easy one to point to because, one, there's been some bad practices. But secondly, it's an easy one to point to because most people don't really care, if it costs \$100,000, they don't really care that it costs \$10 million to develop, right?

And so I think that, as entrepreneurs running our businesses, if we want to help drive drug costs down, the first thing I think we should all think about hard is dollar-one coverage. Move away from these high deductible plans because all we're doing -- yes, we're lowering our own costs with our companies -- but all we're doing is just shifting that burden onto our employees. And so some fundamental things need to change there.

What does concern me is the fact that we've outsourced most of our manufacturing capabilities to China and other places. We saw some of the impacts of that during COVID. And starting to domesticate some of those development or manufacturing companies here in the US and in Europe. We cannot be reliant on one country to do most of our manufacturing from a drug substance and manufacturing capability point of view in this area. And so that needs to be de-risked.

And I think that what's interesting is that, if you look at today, China, they remain a fast follower market. I don't know if that's always going to be that way. I hope for human health that we're continuing to challenge each other and make each other better, but I also think that there is -- part of the reason why my new company is in stealth, we're not talking about what we're doing, we raised \$400 million and didn't tell a single investor what we're doing. We said, hey, we're going after precision immunology. Here's the broad areas we want to play, but this is a bet on us and a bet on that strategy.

Dan Dees: Raised \$400 million that quickly.

Mark McKenna: Yeah.

Dan Dees: Wow.

Mark McKenna: And where I was going with that, though, is that the minute we disclose what we're doing, there's going to be ten companies in China just mimicking what we're doing. I don't think that's helpful. Now, there are patents in place and all that, but with antibodies it's small tweaks on the sequence and next thing you know you've got freedom to operate.

So these are some fundamental things that are impacting drug costs. And honestly, it's survival of our species. If we don't have the ability to stop manufacture of a vaccine during a pandemic, that's a problem.

Dan Dees: Yeah, got it. In the couple minutes we have remaining, I want to get at you've said speed is the new currency in biotech. I think that's applicable across entrepreneurship more broadly, so I'd like you to apply that more broadly but also get at in biotech, it strikes me as something that is exciting and definitely true but also comes with risks. I don't know how speed plays with safety

and all these other things, so give me a perspective on all that.

Mark McKenna: As everyone knows, you can either do things in parallel or you can do them sequentially. And I think that what a lot of entrepreneurs I think struggle with is they follow a process. And I think you got to take a step back and say what is the cost of -- you know, what is my burn rate on a monthly basis? Right? And my burn rate may be, you know, \$3 or 4 million. So am I really going to skimp over here and save \$500,000 where I can run things in parallel versus sequentially and be able to answer hypotheses much quicker?

Developing drugs, it's all about hypothesis generation and being able to, "Well, hey, is it agonist or antagonist? Do I need to bind to this epitope or that epitope?" So there's a lot of iteration that needs to happen. Being able to do some of these things in parallel together at risk is a lot cheaper than running them sequentially when you figure in your burn rate. So that was what I meant by that comment.

What it does not mean is cutting corners. What it does not

mean is trying to find -- you know, putting safety of patients and others by the wayside. The way we look at this is that there are 5 million patients out there that are struggling with inflammatory bowel disease and other autoimmune diseases. Getting these drugs to patients as fast as we can is going to change lives, so inherently we're going to take risk. And we're probably going to take risk in ways that big pharma wouldn't. And all that means is we're going to run these two experiments at the same time and we're going to be thoughtful about how we do that. But then we're going to be able to make decisions much faster.

About 75% of the drugs that are in the market today did not originate in big pharma. They're originating in small companies. And then they're eventually sold to bigger companies to run the larger clinical trials that need to happen. But the minute we sold the company to Merck, they're like, "Okay, we're doubling the size of the patients. It's going to take an extra four years." And some of that's good. You need a little more rigor and probably sample size.

But on the flip side, you're extending the time of these

drugs to get to patients by several years. The start to finish of these drugs is mostly about ten years. So the product life cycle is very, very long.

And if I could just make one other comment because I know we're out of time here, one of the earlier panels was talking about generative AI and kind of how that's impacting tech and other areas of the economy. I think that AI and machine learning, deep learning, has the ability in health care to change the space more than anything else that we've seen in the last 100 years.

Data is power here. And given the response rates, if we're able to start to stratify patients and understand, hey, which genetic phenotype is actually more likely to respond to a particular drug, that's meaningful. So the last company I sold, we had a dataset of 20,000 patients. Blood, tissue. It was paired with clinical metadata. All that means is, like, we see the history of the patients over time, right? So you can really start to identify who's a responder and not a responder to a particular drug.

We're doing things now that didn't even exist two years ago. One example -- and again, we're still in stealth -- but we've

been able to take all the pub med articles that have been published in our area and put them into our own ChatGPT system. So now we're not relying on one scientist to remember that that particular variant was important to this particular disease area. Right? Because it's not completely obvious.

And so the machines are actually helping us. We can, in our own environment without anyone else seeing, ask questions about different mechanisms. And it'll help us synthesize that information. So again, it's not reliant on one or two clinicians to help interpret it for us.

It doesn't stop there. It's not going to be 100% foolproof obviously. But we're doing things today that didn't even exist two years ago. And that's what gets me so excited about curing cancer, curing autoimmune diseases, and being able to leverage ethos to probably drive longevity in the next 20 years.

Dan Dees: Hurry up. Hurry up. No, congrats again on the success. I love the scope of your ambition. I love the progress you're making in medicine. I appreciate you sharing your perspectives here. I know you're going to be

here I think for the rest of the day, so you can continue to share those views. But thank you for all you're doing.

Mark McKenna: Thanks, Dan.

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