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**Announcer:** The *BioWorld Insider Podcast*.

**Lynn Yoffee:** This is the *BioWorld Insider Podcast.* I'm Lynn Yoffee, BioWorld publisher. Our guest to day is Mark McKenna, the CEO of Mirador Therapeutics. Mark was the CEO of Prometheus Biosciences in 2023 when the company was sold for $10.8 billion to Merck. He found that he could only sit on the sidelines and watch for a very short time. He jumped right back into drug development less than a year later by launching Mirador with a $400 million seeding.

That's one of the largest financings so far this year. The company is taking a tailored approach to developing therapies for immune-mediated inflammatory and fibrotic diseases. He has a lot of experience starting at Johnson & Johnson, then at Bausch & Lomb for more than a decade, and later as a president of Salix Pharmaceuticals. Welcome Mark.

**Mark McKenna:** Thanks, Lynn. Appreciate you having me.

**Lynn:** Mark is here today to talk with Lee Landenberger, BioWorld staff writer and the BioWorld Insider host. He's talking about Mirador and the pharma landscape in general. Over to you, Lee.

**Lee Landenberger:** Thanks, Lynn and Mark. Thanks again for joining us today. You and I talked in late March when Mirador launched, and it was a great conversation. It was wide-ranging, and I thought, why not talk some more with you? I invited you on the podcast, and you were nice enough to say yes, so welcome.

**Mark:** Well, I enjoyed the initial dialogue as well. Thanks for covering the launch of Mirador Therapeutics, our new company. We're beyond excited for the potential that this could provide for patients that are suffering from chronic immune-mediated diseases. We're excited to get the band back together and complete the mission. Thanks for having me here. I'm excited to talk about all things Mirador, walk you through the Prometheus journey as well, and discuss, as you said, wide-ranging issues in pharma and healthcare.

**Lee:** Yes. Let's launch Mirador right now, again. You raised $400 million to get the company going, and that's one of the largest financings of the year. How'd you go about that in such a tough market?

**Mark:** Yes. It was very different than the first go-around with Prometheus, where we didn't have the established relationships. We didn't have the track record. We didn't have the team assembled. In this situation, I think that what started out as an idea in my family room with my chief scientific officer later became a full-blown company. I think that, over the summer post the exit of Prometheus, many of us had some social searching to try and figure out what we wanted to do when we grew up.

For me, while there was a lot to weed through with regard to different opportunities, both board and operating roles, to me what it came down to is there was a lot of unfinished business at Prometheus. There was a team that was in place that was a well-oiled machine, and we started having conversations with investors about raising $100 million or $200 million, and what we found out is that there was incredible enthusiasm for what we could potentially build together once again as a team.

That really laid the groundwork for where we landed at $400 million. More important than the $400 million is the fact that there was a lot of enthusiasm around immunology and precision immunology and what could be in terms of cracking this efficacy ceiling. Today, you look at multi-billion dollar drugs like Humira, they still are providing sub-optimal efficacy levels to patients in key areas like inflammatory bowel disease, RA, and others.

For example, in inflammatory bowel disease, Humira provides 10% to 15% clinical remission. That means that 85% of patients are not currently having their needs met, and they're dealing with a very chronic debilitating disease where many of them go to the bathroom 10 to 15 times a day. They know where the restrooms are on the way home from work.

This impacts everyday people. This is not a rare disease. There's million people globally that are afflicted with inflammatory bowel disease. The idea that we were going to just provide one treatment and be done, I think we can do better. I think that, with this 400 million, I think there's plenty of ways that we can continue to improve the efficacy for these patients and change lives.

**Lee:** Talk to me a little bit, if you would, about the science behind the company and what the mechanisms are that you're working with. I assume, it's sort of a background follow-up question to that, is that why the company appears to be so valuable to investors?

**Mark:** Well, we're still running somewhat in semi-stealth, and today, I think when you disclose what you're working on, particularly given the success that we've had, you're going to have many fast followers behind you, many of which are coming in China and other parts of the world. We've been very careful about what we shared and who we shared it with.

I would just say that, for those large check writers in our financing that did get some visibility, clearly, a lot of enthusiasm for the potential of what we were building. We've been very careful about how we're disclosing what we're working on. What we said more broadly is there are key clusters that we want to focus on as Mirador. We want to focus on the GI tracts, the lung, particularly lung fibrosis, as well as the skin.

I think that there is a ton of unmet need in those areas. We're not trying to be all things to all people, but what we are going to be doing is following the playbook that we wrote, which is we want to take a genetic approach to drug discovery and bring precision medicine from end to end. What I mean by that is this will be the first time that someone takes a drug in terms of the discovery effort, to the indications that are selected, to how you develop either the chemistry or the antibody, to how you run the clinical trials in terms of patient enrollment, to stratification on the back end, where you think about whether it's a complementary diagnostic or some other way to stratify patients.

This is what we talk about when we say end to end, where it's really not a one-size-fits-all drug, but something that is tailor-made for that particular patient. I think the playbook is clearly there in oncology, maybe not perfectly perfected. There's a number of notable differences, mainly that we're not looking for one association. We're looking for polygenetic signatures in most cases, and we're looking for functional genomics as well.

Look, there's ways to even involve precision medicine in terms of stratification even beyond that. That's exactly where we're going, is where is this market going to be three to five years from now? We want to absolutely be the market leader in terms of precision immunology. I think we have the team capability. We have the data to be able to really pioneer this space.

**Lee:** You had mentioned that clinical trials would be smaller. That's the way you envisioned them for the company, instead of much larger ones. That means less money spent and less time in development. Is that right?

**Mark:** Yes. I think that's at the core of the thesis here, is that, by having a more selective enrollment process, you can run smaller trials, faster enrollment periods, less cost. The playbook for that is in oncology. I think what we've yet to ... this is still being digested by regulators in the other areas outside of oncology. As you start to bring forth transformational therapies that materially move the needle, I think that's how you're going to start to see more rapid type of approvals and access to the markets.

I think a good case study here, as you look at cell therapy, there's a lot of promise in this area. There's a lot of risks that are still ahead of us. You think about areas like lupus, very severe patient populations. You have potentially curative treatments in cell therapy, but are they going to-- when you're getting 75%, 80% remission rates that are durable over a year, are you really going to make them follow a traditional development path? I personally don't believe so. Time will tell what that looks like.

I'm incredibly excited for the opportunity to bring forth data that is going to change the way we develop drugs in this area. There's an alternative agenda here. Obviously, we're patient focused, and we believe that we can do better for these patients. We believe we're the best hope for bringing forth transformational therapies in this area. That's why we're back at it.

The other agenda here is immunology is the number one drug spend category in the US. If you actually want to tackle drug spend while getting patients better outcomes, which I think is the panacea that everyone talks about. I believe that there's really three ways to do it. One is new MOAs, new drugs that provide differentiation. Number two is precision medicine, where you identify subsets of the population that can benefit from a particular drug. Then finally, combination therapy.

We intend to tackle all three of those over time, but if we're able to move the efficacy bar in this area, it's going to result in huge drug savings, cost savings, while still giving patients better treatment options. That gets me excited.

**Lynn:** I'd like to jump in here with a question, Lee.

**Lee:** Yes.

**Lynn:** Mark, so when you start talking about tailor-made drugs for patients, and obviously we want better results for those patients, you start thinking about very expensive therapeutics. Are you already planning on pricing at this stage and how to position that in terms of value?

**Mark:** Yes. No, it's a fair question. I think that you're absolutely right that, historically speaking, when you go after rare diseases, given the limited patient populations that you're going after, oftentimes you see these drugs that are very expensive. I would remind you that there's 5 million patients globally that have inflammatory bowel disease. If you find a drug that works in 20% of them, that's still not a rare disease. All that is, a way to get to those patients faster.

The agency should reward these type of initiatives because they result in better patient outcomes and as well as cost savings. To me, this doesn't have to be a rare disease type of scenario, particularly when you're going after these very large markets. I think that we're always going to price for value, but the strategy going in is not setting up a market that can be nefariously exploited. It's quite the opposite. It's like, there's a huge problem out there that has been unsolved.

We brought forth very expensive treatments that are basically hammers for the immune system. We found that those don't result in materially different outcomes. I think the Humira case study and all the other agents that have followed is the case study that we should look at. We should talk more about this on a separate podcast or later in this podcast, because I think there's just a lot of misinformation about pharma pricing and pricing for value. The strategy here is better outcomes, lower cost.

**Lee:** Oh, I'm happy to talk about it now if you'd like to. Did you have further thoughts?

**Mark:** Yes. I mean, I think that over the last 20 years in various political cycles, we've seen this rhetoric around pharma pricing. Don't get me wrong, there's been a few bad actors. That being said on whole, the innovators in this space have been agents for change and for good. Without them, we wouldn't have solved the COVID crisis. We would still be wearing masks every day.

I think that, when you take a look at what's broken in our system today, it's not the innovators. What is broken is our system, where you have middlemen basically, collecting rebates, taking, apparently, allegedly negotiating on behalf of employers, but taking these massive rebates, acting as middlemen where they provide next to no value in the system. I'm talking about the PBMs.

I've seen firsthand working in this ecosystem over the last 20 years, negotiating with the payers, how flawed our system is. Until we actually deconstruct that, we're not going to get to a situation where we have healthcare for all, and we're not going to get to better treatments for patients. I think we should be rewarding the innovators. The last comment I would make in this space is that this is the one of the few segments in the American economy where the U.S. is still the undeniable market leader.

Do we really want to outsource our R&D to other places around the world to either friend or foe? I think that we should think very carefully about that. Rather than demonizing those who are actually doing-- spending billions of dollars at risk to bring therapies to the market, let's reconstruct the market and take out the middlemen who provide no value in the system, yet extract a disproportionate amount of economics out of the system that could go to lowering drug prices.

**Lee:** Were you seeing that at Prometheus or even probably earlier? I'm curious when that first became something in your sights.

**Mark:** I think I had an aha moment when I went to Prometheus, going from a large pharma company to a biotech, where trying to raise capital and fund these large development projects, there was a realization that there is an extraordinary cost to bringing these drugs to market, over a billion dollars in many cases or more to get these to market. A lot of the times, this is binary. The drug either works or it doesn't work.

Yes, you can get something that's on the margin, but I don't think that's what any of us are playing for. We're playing for transformational therapies. Yes, coming into the biotech arena where you have to raise capital, and every dollar that you spend is precious, you realize that drug development is extraordinarily hard. It's super expensive. It reinforced what I saw on the other side at large pharma negotiating with the payers where incentives are not aligned.

I think we need to focus on what's best for patients. I think that this idea of bringing precision medicine into immunology is a great way to reduce drug costs and improve healthcare outcomes.

**Lee:** When you were putting Mirador together, was that part of the plan? Because you brought back a lot of execs to work with you from Prometheus. Was this a part of your discussion?

**Mark:** No question. I think that the broader strategy and unmet need that remains in this market was the underpinning for the company and really, the thesis behind why we exist. Mirador in Spanish means the vantage point, the lookout. We believe that, based upon what we've accomplished together as a team and the data that we have via Mirador 360, which is our proprietary dataset, gives us a unique view on immunology and the immune system.

We're not just developing one drug against one target. We're doing drug discovery through this large dataset where we're looking for-- leverage this asymmetry of information that we have to bring forth new therapies, new mechanisms, new precision approaches. To me, the secret sauce here is the team. We coupled that with some of the world's leading investors, Arch Ventures, Orbimed, Fairmont Funds, along with, a dozen other top-notch investors, Fidelity, Point72, Woodline, Venrock, so on and so forth, so many to name.

These are the innovators in the space that are making the bets on entrepreneurs and making the bets on science. When you couple this team with this capital, this group of investors, this board that we've assembled, man, this could be a lot of fun. The aim is to transform outcomes for patients in this area. I think if we focus on inputs and building a great company, no doubt great things are going to come.

**Lee:** Last month, you and I were talking about the economic landscape for companies operating in pharma. At the time, you said that the market looks fundamentally different today than it did a few months ago. I think what you meant, that was a sign that you felt better times were ahead. We felt like the Fed was going to tamp down interest rates. Now, inflation is still more of a thing than thought even a month ago. Do these new numbers change your outlook at all?

**Mark:** I think in the last 30 days, you've seen a retrenchment in the XBI. The majority of that can be attributed to the rising or lack of deflation. When you look at biotech, it's highly correlated to interest rates. Why? Because none of these companies are actually generating-- or most of them are not generating a profit. These are investment intense businesses that require lots of capital at risk.

When interest rates go up, it has a negative impact on the XBI, which is the biotech market. Yes, I think that we are far from out of the woods here. I'm not an economist, but I would say that seeing it firsthand here on the ground, you're seeing a bifurcation of the market where those that have A-plus science and A-plus teams are able to raise money.

Those, with less track records or less compelling science or focusing on areas that are not in vogue are more challenged to raise capital. I actually think that's pretty healthy. the juxtaposition to that would be 2020 and '21, where capital was free flowing and every company was getting invested, getting funded. I'm not sure that's a healthy market. You just take a look at success rates in biotech. If you're sprinkling bets on every company, eventually the music's going to stop there. You got to go be more proficient at picking winners than losers.

I think that the rise in interest rates, the challenges in the market of creating, two different worlds where, again, certain companies can easily raise money and others have more challenges, I think long-term this works to the benefit of the market because we're getting the better science funded and seeing more consolidation in the space on teams and science.

**Lee:** Okay. We've covered a lot of ground and we could probably drill a lot deeper on some certain topics. Is there anything, Mark, that we have not talked about that you'd like to mention?

**Mark:** Yes, I think one of the things that we should dive into more is like the outlook going forward. I think this is a question I get a lot from investors and from other journalists is, what's going to happen in the market as you think about the loss of exclusivity and some of the pressures that face the big pharma companies over the next 10 years? You take a look at the fact that, between 2023 and 2030, these large companies are going to lose circa $320 billion in revenue as a result of LOEs where their patents expire.

What does that mean for the market? For me, I think that, again, this is healthy, but it's also going to require them to restock the shelves with innovation, both organically and then also through acquisition. I suspect that there's going to be-- continue to be a lot of M&A in the space in order to replace the revenues from key drugs like Keytruda and Humira, other multibillion-dollar drugs.

The Inflation Reduction Act, which was passed about 18 months ago, two years ago now, puts further pressure as it creates another challenge for these pharma companies, particularly those that are working on small molecules to recoup their investment in a shorter period of time. I think that the IRA is probably having an opposite effect with regards to, one, reducing inflation, and two, actually lowering drug costs because it's doing it in a way that provides perverse incentives and has drug developers not pursuing the best science.

As I mentioned earlier, there's a way to do this where it can improve outcomes and also reduce costs. I think that the last thing I would say is that this ecosystem, there's probably a misunderstanding of how the ecosystem works, particularly amongst regulators. This is not a typical market where you see consolidation being bad. You actually need consolidation in order to create a healthy market.

Given the amount of capital that's needed to run large phase three trials, that's oftentimes not best done by a small biotech company, but rather by a large pharma company who has the know-how and resources to do that. We've seen intense pressure by the FTC over the last two years to push back on various deals in the segment. I think a lot of times it comes-- the impact there is it's negative for patients, and it's negative for the ecosystem. We coexist together and need one another to be successful.

It's unlike other areas in tech where consolidation can lead to monopolies. One of the biggest travesties, I think, in healthcare that I've seen in the last 20 years is allowing the payers to vertically integrate, where you have the PBMs and the health plans and the pharmacies all being owned by the same entity. How do we allow that to happen? Yet we're worried about one pharma company buying another company where there's plenty of competition in the market.

Once again, these are like large problems that we need to sort out together. I think that a active M&A market is very healthy for biotech and for patients.

**Lee:** Got it. Man, this is great. We could just go on for a while here, but I think this is a good time to stop. Mark, I really appreciate your insights and I want to wish you the best of luck, you and everybody else at Mirador. I look forward to talking to you when you get into the clinic.

**Mark:** Sounds good. Lee, thanks so much. Thank you, Lynn, and look forward to chatting again very soon.

**Lynn:** Mark, thanks so much for joining us today. We certainly look forward to covering all of the incremental updates in BioWorld. That's our show for today. As always, BioWorld will continue to keep you informed of all the most important scientific, clinical, regulatory, and business updates.

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