**Speaker:** The *BioWorld Insider* Podcast.

**Lynn Yoffee:** Welcome to the *BioWorld Insider* Podcast. I'm Lynn Yoffee, *BioWorld*'s publisher. It's that time of year again, we're reflecting on 2023 and importantly, looking ahead to 2024. What were the most impactful events, and are they catalysts for upcoming changes in the new year? We asked six prominent biopharma CEOs to tell us what they're excited about, as well as their concerns. This episode also provides a preview of the annual Biotech Showcase conference, an investor meeting for private and micro to mid-cap biotech companies.

The event has really grown substantially and is an important gathering adjacent to the JP Morgan Healthcare Conference in San Francisco. This year, BioWorld is a sponsor of the biotech showcase, which is happening January 8th through the 10th. If you attend, you'll have the chance to hear panels and join workshops and fireside chats with key opinion leaders, just like the CEOs we're interviewing today. Podcast host and staff writer, Lee Landenberger, had some great discussions with CEOs.

**Lee Landenberger:** Yes, there were six of them. We spoke with Dave Bearss, the CEO of Halia Therapeutics, which is focused on developing treatments for inflammatory disorders and neurological diseases. We spoke to Vimal Mehta. He's the CEO of BioXcel Therapeutics, a company that's leveraging artificial intelligence to develop neuroscience medicines. Paul Lammers, the CEO at Triumvira Immunologics, which is developing autologous and allogeneic T-cell therapeutics aimed at solid tumours.

We talked to Chris Pirie, the CEO of HDT Bio, which is seeking to harness host-directed immune responses with a focus on infectious diseases and oncology vaccines. Thijs Spoor, CEO for Perspective Therapeutics, a company focused on cancer treatments that use radiation radiopharmaceuticals and imaging technologies, and Shelley Hartman, the CEO of Aegle Therapeutics, a regenerative medicine company aimed on rare diseases.

**Lynn:** A terrific group. Lee, let's start with a look back.

**Lee:** A look back at the past year that one thing that just about everyone in this group of CEOs agreed on was that 2023 was a tough year financially. Here's Dave Bearss talking about 2023's financial performance.

**Dave Bearss:** I think this past year has been as hard as it's ever been, maybe the hardest it's ever been in terms of attracting new financing. There's a lot of reasons for that, but the public markets have been completely closed and I think the performance of companies in terms of their stock performance has been very poor, but it's also been just an incredible time. We see some amazing things happening right now.

**Lee:** Shelley Hartman weighed in on the public markets.

**Shelley Hartman:** Lee, as you know, the NASDAQ Biotech Index is off by I think around 7% since the beginning of 2023. I do think there's some good news in that the deep price declines that we experienced in the sector between, I want to say September '21 and mid-'22, have stabilized somewhat. That being said, only a handful of biotech companies have gone public in 2023. Unfortunately, the class of '23 biotechs have not performed well as a group. There have been some terrific success stories there, but in several cases, the data was not positive, which of course, continues to put investors on edge.

**Lee:** Chris Pirie had a bit more positive view, albeit from the Northwest Seattle bubble.

**Chris Pirie:** Generally speaking, our industry has performed quite admirably in the past 12 months or so. We've faced some broader economic headwinds, but I see around me here in the Seattle ecosystem and a broad, founders continuing to stay the course in earlier-stage ventures like ourselves. We've seen the big pharmas really holding the course in terms of value creation in our industry with respect to either marketed approvals and commercial, value recognition as well as M&A.

All of that is not to make little of the fact that we have seen challenges in what I would call the middle market in terms of publicly traded companies that have struggled with financing. You've seen a lot of the strategic reorganizations, reverse mergers, and even shuttering that does have the effect of dragging a little bit on the industry, but from our perspective, it recycles talent into those ventures that are showing the most promise and even new ventures, as the case may be.

**Lee:** Thijs Spoor spoke about Big pharma's massive amount of cash on hand.

**Thijs Spoor:** I look at a company like Novo Nordisk with so much cash on the balance sheet, so much commercial success, they're in the middle of closing a transaction with a company I used to be the CEO of to acquire a really interesting drug in blood pressure. That deal is projected to close in this quarter for $1.3 billion for a really compelling asset in hypertension in patients with chronic kidney disease.

There are chronic diseases where phenomenal innovation is happening, and the rewards are there both for the patient payer-provider in terms of benefits, but then also for the manufacturers in terms of proprietary products where the health economic argument is more than justified with the advances there being made. What happens with all that cash? There's a great analysis I think that Stifel did a week ago saying there's so much cash sitting on Big pharma's balance sheet. They could almost buy all of biotech.

**Lynn:** Now, in terms of technological breakthroughs that will resonate in the coming years, GLP-1 agonist is weight loss drugs, CRISPR and ADCs were all key advancements. First, we have Dave Bearss who went right to the weight loss drug phenomenon.

**Dave:** There's been a huge revolution of new breakthroughs that are leading to new ways to treat diseases that we've been after for a long time. Probably, the top-of-the-mind one is what's happening with the GLP-1 agonist and this massive thing that's just exploded that we see for type 2 diabetes but also just for weight loss. I don't think we've ever had an opportunity where literally a billion people in the world could be the target for a new therapeutic.

I was chatting with somebody from Novo Nordisk, just one of the scientists there. It's amazing how when you have a breakthrough like that, it's hard to project what's going to happen. Certainly, they didn't see the uptake of this, and especially people paying out of pocket to get access to a drug. That's really never happened before where people are happy to say, "You know what, I don't care. The insurance company doesn't have to reimburse. I'm going to pay out of my own pocket." Those types of things are really hard to predict, but it's just unbelievable just the groundswell of interest. The fact of the matter is it's because it works. It really is a big breakthrough.

**Lee:** Vimal Mehta jumped on the artificial intelligence revolution.

**Vimal Mehta:** Recently, we are seeing a lot in the space of artificial intelligence approaches being used. The reason for that is the look, our body is very complex. No single discipline can understand everything. If you're a biologist, you understand biology. If you're a chemist, you understand chemistry, but Body doesn't work like that. It needs multiple disciplines integrated together. Any technology that helps us do that has an advantage.

We see that artificial intelligence approaches are independent of individual expertise and agnostic of those expertise, and they can integrate what knowledge is in front of us and bring it to the experts that experts can use. I think new technology combination and also breakthroughs into the therapeutic areas like cardio-metabolic field, that's happening, and particularly, with GLP-1 innovators. That's a very big advance as it can make a big impact on the society. Some of these are very chronic diseases, and now we have some drugs.

**Lynn:** Paul Lammers expressed one of many concerns about artificial intelligence, and he noted the importance of ADCs.

**Paul Lammers:** Scientific and medical journals are struggling and try to provide guidance for reviewers of peer-reviewed articles on how to discover, how to deal with ChatGPT work. The biggest issue is also as companies, we need to train our employees on the potential risk of using ChatGPT because if you draft a paragraph and you're asking ChatGPT to improve that paragraph, suddenly, whatever is in that paragraph, including potential confidential information is in the public domain.

People don't realize that, but I think there's a huge potential risk associated, especially in the scientific discovery field, that people put something inadvertently in the public domain before even realizing it. ADCs right now are the hottest things in oncology. Again, everybody wants to have either their own internal ADC discovery and development process bringing it in from the outside. Again, that's great because these products do amazing things for patients with very difficult-to-treat cancers, which is awesome.

**Lee:** Turning to the year ahead, these CEOs were all hopeful that 2024 would be better financially. They felt that the US presidential election would be a factor in the markets, along with regulations including the Inflation Reduction Act, the hope that interest rates would drop, along with technological advancements such as CRISPR and mRNA, and the troubles that include drug shortages. Shelley Hartman has an optimistic view that 2024 will be a good year for both deals and stability.

**Shelley:** I think there is been so much investment and so much progress at such an accelerated pace that I think 2024 should pan out to be a good year. I think if we see a couple of sizable M&A transactions or material licencing deals, that would provide some real positive momentum, and then of course, some IPOs that are strong performing, that will do a great deal to mitigate investor fear. I'm positive on 2024.

**Lynn:** Paul Lammers pointed to the world news that really has everyone on edge.

**Paul:** There's a lot of things that have happened in the last, say, two years, of course, the Russia-Ukraine War, and now of course, Israel-Hamas. All of that makes people a bit skittish not only about their own wallets and their own households' financing, but also, in general, about where do we invest. I think that the VCs, if they have a really exciting technologies, they're willing to put big Series A in place. Early investing is good, but that's way before you get into the clinic.

**Lee:** Here's Dave Bears highlighting political tensions in the US.

**Dave:** We're facing a general election for president in the United States. That certainly has an impact on the direction of the country economically. I think there seems to be quite a polarised situation in our country right now. The very different approaches to where we're headed, and I think that creates uncertainty for people.

**Lynn:** We go back to Paul Lammers who noted the importance of CRISPR technology as well as its concerns.

**Paul:** CRISPR, it's a fascinating technology. Obviously, it didn't lead to a Nobel Prize for nothing. I really think it's a game changer and a way that we can try to correct genetic mistakes, and/or put something new into DNA to try to get that expressed as a different new protein. The biggest issue for people and **[unintelligible 00:12:30]** concern is there's quite a few technologies out there. Which is the one? Which is the most accurate? The most trusted one?

Obviously, editing genes is great but there is a potential slippery slope. You might go to induce something that was totally inadvertent. The question, of course, is how do we fully understand? I do feel that some companies go too far, and it feels a bit like *The Boys from Brazil*, where we're trying to do so many things, but what are we trying to do here? If you say, well, we have cells, we do five knockouts of genes and we put three knock-ins, I'm thinking, guys, we're starting to play God here? What are you trying to do?

The body also is really smart because the body discovers pretty quick if there's something awkward with these cells. You don't want to have major toxicities and potential life-threatening events happening. I think that's the challenge in the whole field of gene editing, including in CRISPR, which ones are the most accurate, the most targeted, and the safest?

**Lee:** Vimal Mehta warned that if we cannot adequately address diseases like Alzheimer's, then patient care issues will continue to escalate.

**Vimal:** For a while, it was very difficult to have good probability of success for the neuroscience drugs because understanding of underlying biology was not that deep. As it's evolving and new technologies are coming, and new understandings are coming up with these technologies' direct implication, you can impact now the diseases like Alzheimer's, you can impact the diseases like bipolar, schizophrenia, and new drugs, new technologies.

Focus seems to be more on disease-modifying, but at the same time, if those problems cannot be solved, particularly in Alzheimer's, there is a huge need for solving the symptoms where there is a-- Most of the time, patients of Alzheimer's end up in the nursing homes or higher standard of care, not because of their underlying cognition that contribute to certain symptoms in Alzheimer's that results them to go from their loved ones at home to these high standard of care.

**Lee:** Chris Pirie summed up what's been on everybody's mind. We had this incredible industry boom during the COVID pandemic, but now what?

**Chris:** We had a millennium-level event and people flooded into our industry because rightly so, we were saving the world. It was an incredible thing we saw, but like any flood, there was a pullback. It'll be really interesting to see how much of that interest returns. I think some of it will depend on just how effective we as an industry can be of demonstrating in lockstep, successive demonstrations of these new modalities. Indeed, it was sort of traditional mRNA technology that came to save the day in large parts. We need to see more of what that technology and modality can address in terms of solutions for other not-so-pandemic diseases. That, I think, will drive the scope of the return.

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**Lynn:** Thank you to all the CEOs who shared their time and expertise. We actually had a lot of material that had to be trimmed to fit this episode, but you can hear from all of them at the upcoming Biotech Showcase during Biopharma's biggest week of the year in San Francisco. BioWorld is a sponsor at Biotech Showcase. Stop by our booth for some swag and a very special discount to subscribe to BioWorld, the industry's longest-running and most trusted news source.

That's our show for today. We're wishing everyone happy holidays and a great new year ahead. As always, BioWorld will continue to keep you informed of all the most important scientific, clinical, and business updates. If you need to track the development of drugs and medical technologies, turn to bioworld.com. You can follow us on LinkedIn and Twitter, and you can email us with your news and tips at newsdesk@bioworld.com. Don't forget to subscribe to our podcast, which is available on all the top platforms. Thanks for joining us.

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