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**VO:** The *Bioworld Insider Podcast*.

**Lynn Yoffee:** This is the *Bioworld Insider* podcast. I'm Lynn Yoffee, *Bioworld*'s publisher. The year's biggest cancer conference begins this Friday in Chicago. The American Society of Clinical Oncology, also known as ASCO, is an annual gathering of investors and drug developers. It'll be a litmus test, not only of the science of new cancer treatments, but also whether a surging investment market will continue to strengthen. Our guest today is Chris Bardon. She's a co-managing partner at MPM BioImpact, and she'll be at ASCO, as she has many times in the past. She's a physician and portfolio manager for her firm's BioImpact Equities and the Oncology Impact Funds. She has insights into the conference and the broader market that she'll share with us today. Welcome, Chris.

**Chris Bardon:** Thank you so much for having me.

**Lynn:** She's here today talking with Lee Landenberger, a *Bioworld* staff writer and the *Bioworld Insider* podcast host, about investment trends and what to expect from ASCO. Over to you, Lee.

**Lee:** Thank you, Lynn. Chris, it's great having you join us today. I would guess that preparing for such a huge conference as ASCO probably takes a lot of time and effort. I was curious, when do you start preparing for ASCO, and what is it that you're looking for before you go into the actual conference?

**Chris:** ASCO is one of the major oncology meetings for physicians, for scientists, and for drug development in the field of cancer. This year, usually, what happens is we start to prepare for ASCO when the abstracts come out and we know what interesting data is going to be presented at this year's conference. We do have to start early. We have to start to evaluate all the different drug programs, which will be presenting data, and to figure out which ones we want to listen to.

**Lee:** You were an analyst in the past, so that was probably extremely helpful in doing this and in going through all the abstracts. I'm curious, what kinds of trends are you looking for? Do you have anything in mind before you go into looking at the abstracts? Then once you do, and you've gone through everything, and you're ready for this year's conference, what kind of trends are you seeing?

**Chris:** Yes, so I would say the major trends we're focusing on are a few different platforms. One, ADCs, antibody drug conjugates. This is probably the hottest area of drug development within cancer right now. We are seeing every major pharmaceutical company, plus many biotech companies, working in this space. Now, this has been a little bit slow in the coming. We actually had our first ADC approved in the field of cancer over 30 years ago with Mylotarg, but now the technology has really matured.

We are seeing development across many different indications of many novel targets. What's most important, though, is that we're seeing transformative efficacy out of some of these ADCs. HER2, which is the biggest blockbuster within the field of ADCs, has shown incredible efficacy not just in HER2-positive breast cancer, but also HER2-low breast cancer and even HER2-negative breast cancer, as well as HER2-other positive tumors such as gastric. We're really excited to continue to see the wave of new technology surrounding antibody-drug conjugates.

**Lee:** I guess ADCs are here to stay, and I'm curious, if you were to look back just a few years ago, would you have thought that they could have come as far as they have in the past, say, two, maybe three years?

**Chris:** It's funny because ADCs stagnated for a period of time, where we really didn't see a lot of development in the technology, primarily because we didn't have good linkers and we had limited payloads. That technology has really matured to the point where we can actually generate very stable ADCs, which can be targeted better to the tumor without significant toxicity. The technology has matured and really come of age, I would say. We are seeing now incredible efficacy, as I mentioned, and HER2 is really going to be one of the most transformative drugs in the field of breast cancer. I think we're just opening the door for the next generation of ADCs as well.

**Lee:** Are there any companies and therapies within ADC that as standouts going into ASCO?

**Chris:** Yes. I see, first of all, we're going to see a proliferation of many, many new targets. There's some old targets that we know of, like TROP2. The first-generation TROP2 ADCs were actually not very good in terms of their linker stability, but the next generation looks much more promising. We're also seeing activity in some old targets like PSMA, where we were unable to previously develop ADCs without significant toxicity. Then as well, we're seeing completely new targets as well, such as B7H3 and other targets that we've never been able to address with ADCs.

I think the other forefront of ADC technology will be new payloads. Part of what we saw in this current revolution is the use of topo-inhibitors for conjugating with ADCs. In the future, we'll see conjugation with all kinds of molecules, including immune activators, including degraders, including targeted therapies potentially. Theoretically, ADCs can improve the therapeutic index of anything that it delivers. From that perspective, there's tremendous promise in this class.

**Lee:** Okay. In addition to ADCs, what are some of the other hot technology trends in cancer?

**Chris:** One of the other actually major payloads that we're just opening the door on, which is akin to an ADC, is actually called radiotherapy. Radiotherapy is where instead of using a chemotherapy payload, that you actually use a radioisotope as a payload. The first generations use lutetium therapy, but now, we're seeing new data with alpha emitters as well as with new targets. The first approved therapies were in PSMA as well as somatostatin, but now we're seeing new data on alpha emitters with non-PSMA targets. We think this is going to be very exciting, especially in the field of prostate cancer.

**Lee:** Are there any particular companies that as being in the forefront right now?

**Chris:** Yes. J&J, for example, and their part in actinium, will basically be presenting a phase one data for a new target called KLK2 and CD33. We're really excited about that.

**Lee:** How about progress in cell therapy for solid tumors?

**Chris:** Yes. In general, as you know, cell therapy has been tremendously effective in the field of heme malignancy. We've made dramatic progress with CD19 in the field of DLBCL as well as ALL. Then we've also made progress with BCMA in the field of multiple myeloma. Now, what's new is cell therapy in the field of solid tumors. Of course, this year we had the first approval of a cell therapy in a solid tumor, which was a TIL, a tumor infiltrating lymphocyte, which is externally purified and then re-administered to the patient.

As well, we'll start to see manipulated autologous CAR T cells for the treatment of solid tumors. We'll actually see the first data of that with the GPC3-specific autologous CAR T for the treatment HCC, hepatocellular carcinoma. We're really excited that this next chapter of cell therapy for solid tumor is just opening.

**Lee:** Okay. Are there any companies that as being at the forefront?

**Chris:** The data that I just described is data from Astrazeneca, but of course, the major players in the space include Kite, Gilead and Bristol Myers Squibb. I think in the future, hopefully, we'll also see development in allogeneic CAR T, and maybe even someday in in-vivo CAR T, where we wouldn't need to manufacture the cells outside of the patient, but rather just to administer the CAR T genetic modification directly to the patient and modifying their T cells internally.

**Lee:** There will be companies that will present on that as well, probably this year. Is that right?

**Chris:** There is actually no patients present. They're not presenting on in vivo CAR T. That's more for the future.

**Lee:** Got it. Interesting. Okay. Artificial intelligence. It's definitely not going away. How does AI factor into the investment landscape in cancer? It seems to me it would be constantly changing, especially recently.

**Chris:** Yes. We're integrating AI into each of our portfolio companies. In fact, last week, at our LP meeting, we had a whole panel dedicated to the different ways AI has impacted the drug development space. First of all, for many years, we've already used AI for intelligence structure-based drug design. Imagine we used to do high throughput screening manually, where we would test millions of different compounds against an assay or a target manually to identify the molecules which responded. Now, we can do that in silico using AI techniques, where we understand the protein structure of the targets and that we can intelligently design molecules for that.

AI will continue to be important for the drug development process. As well, it will help screen drug development candidates for an improved chance of success. For example, we have technology now that can identify toxicity of potential chemical compounds and, hopefully, that improves our ability to predict toxicity in people and, therefore, increases our chance of success.

Additionally, and finally, I think that we will see a ton of AI in the use of clinical trial enrollment and design. Right now, again, we're manually opening sites and designing trials without a full understanding of the type of patients that we will have access to. In the future, basically, all CROs are going to have AI very central to their clinical trial execution process, where you can understand exactly what inclusion criteria you should use when designing your clinical trial, where you know exactly where those patients will be and, therefore, it can enroll sites, which have the highest number of participants, and, therefore, to, let's say, accelerate the clinical trial process and make it more efficient. I think all of these changes related to AI make us more efficient, and that's going to be incredibly important over time because as you know, especially with the impact of the IRA on drug pricing, we need to become more efficient so that we can still maintain our same return on capital, invested capital.

**Lee:** Got it. That covers the ground that I wanted to ask about. Chris, is there anything else that you'd like to chat about, about ASCO and cancer trends?

**Chris:** I think what's also exciting is that we are now starting to see potentially the ability to replace chemotherapy. Chemotherapy has been an old standby in the field of cancer treatment but, as you know, has tremendous toxicity to patients. What's exciting is that, over time, we continue to see replacement of chemotherapy by targeted small molecules, as well as with other better chemotherapy administration methods like an ADC. I think that's very exciting.

The other trend that we're seeing is ongoing use of combination therapies. As you know, we can't cure cancer with any one magic bullet. We need a combination of drugs. Going forward, we will start to see more intelligent combinations of drugs, whether that's IO plus chemo, which we've already seen, but in the future, we'll see IO plus an ADC. I think that's also very exciting to see whether these combinations can yield not just additive, but synergistic efficacy in patients. Ultimately, our goal is to actually develop cures in patients. That, hopefully, is something we can achieve with the new classes of therapies being used in combination with each other.

**Lee:** Got it. Lynn, did you have any questions for Chris?

**Lynn:** No, I think it's really exciting. As always, *Bioworld* will be there at ASCO, and we'll be highlighting the most important updates out of this conference in the cancer space. Chris, we really appreciate your preview today.

**Lee:** Chris, thank you so much for your time and insight.

**Chris:** Thank you so much for having me.

**Lynn:** Thank you for joining us, Chris. As always, *Bioworld* will keep you informed of all the most important scientific, clinical, regulatory, and business updates. Particularly, we will be at ASCO, covering the most important breaking news and cutting through that tsunami of data coming out of the biggest cancer conference of the year.

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