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Paul is the founder of SugarCone Biotech LLC, a consulting firm specializing in the oncology, immunology, and autoimmunity therapeutic areas. SugarCone focuses on the alignment of scientific, clinical and commercial strategy to drive successful drug development. He recently co-founded Vide Biotherapeutics, a biologics based immuno-oncology company targeting select hematological malignancies.

Fiona: The last 12 months have been extremely exciting for immune checkpoint inhibitors seen by the approval of Keytruda and Opdivo. How do things feel at the moment?

Paul: I really feel like we’re in a calm before the storm that will be the medical conference season. It’ll kick off with AACR and then all of the other medical conferences. We’re going to see a huge amount of data in the next 12 months - more indications, combinations with vaccines, with targeted therapeutics, with chemo, radiation. We’re on the tip of the iceberg here in terms of the data that’s coming. We should also see a lot of work on biomarkers, as we try to develop a sense of how to more rationally use and combine immune checkpoint drugs.

Fiona: How did you personally first get into the field?

Paul: Three or four years ago when I was at Biogen I was working on the TIM family members - TIM-1, TIM-3 and 4, and I optioned the program to MPM Capital, a local venture capital fund. I then embedded with MPM, working closely with the investors, executives and scientists, to help them build the asset portfolio that became CoStim. CoStim was then bought by Novartis, in a surprise deal that really signaled to the biotech industry that the immune checkpoint field would become a dominant value driver in oncology.

Fiona: What is the most exciting aspect of Immune Checkpoint Inhibition that you are working on, right now?

Paul: There are a number of exciting projects under way, building next generation immune checkpoint portfolios for companies, a lot of work on novel targets and new technologies - there is a lot of new drug development coming along very quickly.

I think there are several key emerging areas for us. One is to help companies think about how to develop rational combinations. This actually is kind of inherent in the portfolio building space because you want to be able to develop your therapeutic assets together, if you are thinking about rational combinations, which is what you should be doing. I think
there’s strength in that kind of synergy between different assets in the portfolio.

Another aspect of this is better drug delivery, so we are seeing very novel nanotechnology and other technologies designed to enhance bioavailability.

Outside of immune checkpoints, but a field that will likely benefit from checkpoint inhibition, we’re doing a lot of work in the cellular therapies: CAR-T, TCR, TIL therapeutics, gene editing etc. We’re beginning to see momentum in the onco-vaccine space as well. So it’s a very broad remit for us, and very exciting!

Fiona: What do you think the next 12 months hold for SugarCone Biotech Consultants?

Paul: Oh, so that’s an interesting question. Our core to date has really been working on biotech portfolios and assets, and with academic spinouts. What we’re doing a lot more of now, and I think this will become a dominant piece of the business over the next year, is working on the investment side, with investment funds, with VCs, with pharma investment arms, with biotechs looking to invest, to find programs and assets, and to build new companies.

On the flip side of that we’re also now helping small companies raise money - large series raises for the money required for clinical execution. Small private companies reach a point in their lives where they need a big series raise, so the interface between the investment side and the funding side is becoming very important - we can really facilitate matching investment firms and funding needs.

So, novel targets, portfolios, technology, and really a lot of activity in cellular therapeutics as I just mentioned. Also the pendulum is starting to swing back to other areas: core immunology, inflammation and autoimmunity, fibrosis is very big, neurology, some of the neurodegenerative diseases, rare diseases, and pain is another big area. We’re seeing activity build broadly across therapeutic areas.

Finally, our geography is getting very broad, with good connections across the US of course, but our portfolio of clients in the EU, UK, Mideast and Asia is building up rapidly.

Fiona: Where do you feel the biggest challenges in the immune checkpoint modulators field are right now?

Paul: Wow, so I would say that there are maybe three or four that are well recognized. One is that we have to get the response rates up. Immune checkpoint inhibitors are terrific for a small percentage of the patients - 20 percent or less generally.

Two, we have to manage toxicities because one of the reasons the response rates are low is that patients drop out due to tox.

Three, we need to figure out what therapies will work in combination with immune checkpoint therapeutics and right now that’s, I would say, a pretty observational field where people are just trying...
things together. Sometimes they work, sometimes they fail spectacularly, so for the targeted therapeutics (BRAF inhibitors, VEGFR inhibitors, etc) we need to be better at building the rationale for those combos. And all of that, I think, is going to be helped by the development of biomarkers to answer the question: which patients should go on to these drugs.

Fiona: Would you be able to give us a sneak peak of what you’ll be sharing at your workshop in March?

Paul: Sure, so one of our big themes is to talk about the three-legged stool for tumour biology - three ways to attack cancer. This is simplifying the biology dramatically, but it’s a nice model to work with. One leg is the tumour cells themselves, so how do we target the tumour directly. A second leg is the lymphocytes that are attempting to eradicate the tumour, that is our core of the immune checkpoint field, although we have to think about lymphocytes more broadly to include not just T cells but NK cells, perhaps NKT cells, dendritic cells, etc.

Finally, and I think an area of keen focus for us is the tumour microenvironment, which is really an immunosuppressive microenvironment. There are a lot of targets there. Some of them are amenable to small molecule drug development, which would be nice because then you aren’t piling on biologics. You’d be able to maybe have a core immune checkpoint biologic plus a small molecule inhibitor targeting something within the microenvironment. There are a bunch of targets there I really like.

With that in mind I may, if I have enough data, introduce a new company and a new target at the conference. We’ll see how much data I’ve got by then.

Fiona: What are you most looking forward to about the Immune Checkpoint Inhibitors Conference?

Paul: This is what I love about the line-up here. It’s two things. First I really am looking forward to hearing from the large companies about how they manage their portfolio or their portfolio landscape in terms of looking ahead at clinical practice five years out, seven years out, and how do they align themselves with that vision of where they see the clinical practice going. So if we pick a specific cancer indication and we know we’re going to have a set number of assets targeting that indication, how does the company think about strategy to move forward in a way that puts them in a position to bring forward multiple assets, as monotherapies and as combination therapies. I think the large companies have the bandwidth to do that and I would love to hear some of their thinking on that corporate strategy side.

And then from everyone else I’m excited to hear about new targets, new technologies, the sort of thing that young innovative companies and talented academics will bring to the table. It’s going to be a really good mix in my mind, with some really exciting speakers.

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