Laura Benjamin – CEO, Oncologie, China



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Dr Laura Benjamin, CEO of Oncologie, shares the rationale behind their exceptional decision to simultaneously establish offices in both the US and China; their unique biomarker approach focusing on the individual patient's tumor microenvironment; their strategy to differentiate their approaches to in-licensing as well as combination plays within the area of immuno-oncology; and her thoughts on the exciting potential of the China market.

Laura, Oncologie must be one of the first biotech companies to simultaneously establish offices in the US and China. Could you explain why you chose to set up Oncologie in Shanghai as well as Boston?

Our company has two subsidiaries in the US and in China. The reason for establishing in Shanghai is based upon China's fast-changing role within the global healthcare industry. Already, China has joined the US in becoming one of the most important healthcare markets globally. By the time our products become commercially available, the importance of China will only have grown more! Therefore, it makes sense for us to start in China.

In addition, China has had favourable improvements in the regulatory environment. This has allowed R&D companies, such as Oncologie, to include China in our global clinical development strategy at the very inception instead of having to place China on a separate track.

Nevertheless, a company with two main operating sites has to find the best operating model. Oncologie is not simply a company headquartered in the US with a China subsidiary. We want to be a balanced global company across both locations, so we need both sites to work together, yet differentiate their operations in complementary ways. This is why, for instance, we are planning to build a Biomarker Discovery Center of Excellence in Shanghai next year, which will help not only with our current clinical programs, but also our future programs.

Could you share more about the assets you have in-licensed?

We have three at the moment. Our lead asset, bavituximab, is a unique monoclonal antibody that blocks phosphatidylserine (PS) activation of multiple immune cell receptors. The antibody interacts with multiple immune cell receptors involved in pathways that drive immunosuppression. By antagonizing these multiple receptors, bavituxmab can rejuvenate the immune landscape in the tumour, and in that way, provide benefits to patients that have not been able to see the full benefit of the current immune therapies, for instance, patients that did not respond well to PD-1 therapies or those that did but relapsed after a few months.

We currently have two ongoing clinical trials in combination with MSD’s (Merck & Co. in the US and Canada) KEYTRUDA®. One is an investigator-initiated hepatocellular carcinoma (HCC) first-line study which is enrolling in the US. The second is a global study in advanced gastric or gastroesophageal cancer which started enrollment in September and will be conducted in the US, UK, Taiwan and South Korea. The study is designed to be robust enough to fully evaluate our biomarker platform and we hope to have the first cohort of data by mid-2020. We have high expectations of bavituximab and have obtained the global rights for this compound.

The second asset, varisacumab, has a novel mechanism of action to target the Vascular Endothelial Growth Factor A(VEGF-A) pathway with two unique features. The first feature is that varisacumab binds to VEGF-A on a different epitope compared to existing antibodies. By binding the ligand to a unique epitope, we can selectively inhibit the activation of VEGF receptor 2 (VEGFR-2). Equally important is that we have a very robust biomarker validation with previous VEGF-A targeted therapies, so that gives us more confidence that we would be able to identify the right patient population subsets to respond to this compound. Oncologie holds the global rights for this program as well.

The last asset, lefitolimod, is a Toll-like receptor 9 (TLR-9) agonist with a unique structure whose loops have been covalently closed to avoid DNA cleavage by enzymes. This modification gives the

molecule greater stability and allows it to be subcutaneously injected, which means that we would have the opportunity to treat internal cancers that cannot be reached by needles. We have licensed in the Greater China rights for this molecule.

Now, bavituximab actually went through Phase III trials with Peregrine Pharmaceuticals but failed. What did Oncologie learn from that experience?

Bavituxumab was in fact thoroughly investigated in over 500 patients. With Peregrine Pharmaceuticals, their focus had been on bavituximab as an anti-angiogenesis agent, but we do not consider that to be the most interesting or even dominant aspect of this compound. In a robust analysis of their failed Phase III lung cancer study, it was observed that patients from the bavituximab arm that were then given anti-PD-1 antibodies saw a significant positive impact compared to patients from the control arm who were similarly treated. We became convinced that we would be more successful if we changed the focus of the bavituximab development plan to combinations with anti-PD-1 inhibitors. This has led to the initiation of our clinical studies combining bavituximab with Keytruda, and I believe we have a very unique approach here in terms of the mechanism of action.

What do you think is key to having a successful clinical development strategy that leverages your presence in both Boston and Shanghai?

We have a global strategy and we aim to incorporate Asia in our global strategy from the get-go. We have found some very strong development leaders with extensive pharma and biotech experience, both in the US and Europe, but also within the Asia-Pacific region, to guide us through the process. The assets we have in-licensed, such as bavituximab, have prior clinical experience in US, EU and Asia, including Taiwan and South Korea. We can start trials more quickly in these countries to obtain Asian patient data, which will facilitate our eventual entry into mainland China.

Another aspect to consider is indication selection. The drugs in our portfolio could be relevant for a variety of tumor types, but we want to select the indications which would also be relevant to the China and Asian markets. For instance we are, so far, strongly focused on liver, gastric and lung cancer, which are serious unmet medical needs in Chinese and other Asian populations.

Combination therapy is also the focus of Oncologie and this is becoming a major trend in cancer in general but how will Oncologie differentiate your strategy from other biotechs?

PD-1 and PD-L1 therapy is a very hot topic in China, as well as globally, but it is somehow difficult now to differentiate one compound from another. The currently marketed anti-PD-1 and anti- PD-L1 therapeutic antibodies right now may command hefty price tags but in the long run, the intense competition will drive prices down. We are aware that we need to have quite differentiated assets able to form novel combinations, in order to have a competitive advantage within the market.

Both bavituximab and lefitolimod are combination plays with anti-PD-1s and this is embedded in their mechanism of action. We have high expectations that these combinations will improve upon PD-1 monotherapy. Our biomarker approach is a major differentiating factor which we believe is going to help us narrow the population pool to patients that will really benefit from the combination therapy. Understanding the patient population is going to be an advantage for us in terms of clinical efficacy, regulatory speed, and hopefully also reimbursement of pricing when the time comes.

Varisacumab is different, it has opportunities both as a single agent or with a standard chemotherapeutic. Our biomarker is going to help us differentiate from other anti-angiogenesis approaches by addressing patient populations where anti-VEGF agents have not been able to be approved.

Chinese biotechs tend to amass a large portfolio while US biotechs prefer to have only a couple of assets. Where does Oncologie stand on this?

Indeed, many Chinese biotechs are looking to build portfolios with ten or more assets. The mindset in the US is rather different, and it is partly related to the investor environment. For Oncologie, we are actively evaluating additional assets and next year, we plan to add one or two Phase 2 assets with global rights.

In the future, we will look to grow by starting programs at earlier stages of development. Our goal is to be a long-term company with a sustainable pipeline.

Compared to many Chinese companies working with in-licensed assets, our assets, aside from lefitolimod, have global rights and therefore global development plans. These are more significant and extensive in terms of operations and value. We also have our precision medicine biomarker

platform, which allows us to take a drug and differentiate it.

Could you tell us more about Oncologie's biomarker approach?

Our approach to biomarker development is unique. When people think of precision medicine, they think of DNA-based or mutation-based drug targeting, for instance, the EGFR-mutation in lung cancer. They then develop successive generations of inhibitors to block that particular mutation.

We are doing something completely different: we are trying to understand what is actually going on within the specific patient's tumor microenvironment. By analyzing the 'dominant biology' of a patient, we can predict the most appropriate mechanism of action. For example, if their dominant biology is driven by an exhausted immune response, then they are a good candidate for bavituximab. We use an RNA platform to do this because RNA is more dynamic, and with that single platform, we can actually identify patients belonging to specific categories, for which we can develop novel and more effective drugs.

Looking at you personally, you started off as a professor, before going to work at Big Pharma, and now, you have started your own biotech company. What have been your motivations throughout this journey?

When I was a professor at Harvard Medical School, I concentrated on academic perspectives. My work has always been translational and I wanted to publish papers that advocated for better ways to improve human health– but as is typical with academic research, many of the ideas were not implemented. That is what inspired my move to industry.

I worked in Big Pharma first because I believe that, in order to learn the business, from R&D to commercialization, it is better to work in a fully-integrated pharma company. After seven years with Eli Lilly, I decided to start my own company.

One of my favourite aspects of my career in science has been the international nature of it. My PhD was in the US, my postdoc was in Israel and then as a professor, I mentored students from all over the world. Over the years my scientific colleagues, now friends are global, and so am I. This experience made it easy for me to imagine running a multinational company and the global nature of Oncologie is exciting to me.

Seeing that Oncologie has a very unique business model, what would mean success to you in the coming years?

Looking at the biotech landscape, I see that many Chinese companies are looking at the US market. They want to learn more from the US, conduct trials in the US and eventually sell their products in the US. However, in the US, I think the awareness of the Chinese market is very low. That is changing, but in general, many US biotechs or even mid-sized companies have not even begun to consider the importance of the China market, much less strategize to enter it. I think that is a mistake.

For Oncologie, in the coming few years, we strive to become a publicly-listed biotech with a high valuation, having completed successful clinical trials and with registration trials well underway. We are very excited about being able to prove the power of our biomarker platform for patient selection.

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