

Handling a promising cancer agent that keeps on giving, with BeyondSpring's Ramon Mohanlal

By Guy Martin – 2016-11-16

The promise being shown by plinabulin, not just as a natural compound that could provide multiple potential therapeutic benefits in a variety of cancers but also as an agent that mitigates the side effects and improves the efficacy of an established chemotherapy treatment, is enormous.

Many small companies would therefore love to swap places with the immuno-oncology specialist BeyondSpring, which is developing this asset as its lead drug candidate.

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That does not mean that it is straightforward for the company to plot its route to market, but the management team in China and the USA are being innovative outside the lab, as well as inside, to make sure that they develop plinabulin – and any other immuno-oncology drugs that follow it – in a cost-effective and time-effective way.

Chief executive Lan Huang, trained at Memorial Sloan Kettering Cancer Center, is a well-respected researcher and entrepreneur, integrating US and China resources for efficient product development. She set up BeyondSpring in 2013, and acquired plinabulin from US pharma company, Nereus Pharmaceuticals.

BeyondSpring's focus has been on developing the asset for non-small cell lung carcinoma (NSCLC), and increasingly – as the team discovered increasingly potent effects alongside docetaxel in reducing neutropenia – in its use as part of that combination.

Plinabulin's Phase II/III trial for neutropenia prevention with docetaxel currently most excites big pharma drug development veteran Ramon Mohanlal, who was appointed the company's chief medical officer in October 2015.

"Because the effect on neutropenia was so remarkable, we discussed it with the experts in the field – key opinion leaders and the US Food and Drug Administration (FDA) – and we decided to create a separate Phase III program around that," he tells The Pharma Letter.

"So the same drug is now being developed through two separate programs, one in NSCLC and the other in chemo-induced neutropenia."

Aspects which Dr Mohanlal sees as key to BeyondSpring's business model include its focus on small molecule immuno-oncology candidates, rather than complex biologics, and its unique USA-China co-development platform.

BeyondSpring's links with China along with its significant experience interacting with the China Food and Drug Administration and the US FDA ensure fast clinical development speed and reduced costs.

Another key ingredient going forward, Dr Mohanlal knows, will be identifying the right partner, or partners.

"We expect the neutropenia program to be on the market in 2020, so it's important for us that we identify commercial partners that can help with commercialization," he says. "The opportunity comes too quickly for us to be able to build that commercial capability in house."

With plans to take the neutropenia program to the market within four years, and the contacts with regulatory agencies around the world to do so globally, it is no surprise that BeyondSpring has started discussions already with a number of pharma companies which have initial interest. After all, the market is thought to be worth up to \$7.3 billion.

The lung cancer program, which will involve a stronger dosage taken more frequently, will take longer to reach the market.

Dr Mohanlal says: "Currently we have a trial in lung cancer but we will not stop there. There will be a number of other cancer types that we will include in the overall development program. For a small company it's therefore beneficial to have one or more strategic partners so that we can advance these programs sooner rather than later.

"We will be perhaps too small to be able to advance plinabulin in all of these different cancer indications in a timely manner, so there we also would engage in discussions regarding strategic partnering. It could be the same partner as with the neutropenia program or it could be different.

"The overall product proposition to my mind is highly attractive. What plinabulin is doing in combination with docetaxel is that it mitigates a significant related side effect. Docetaxel is an old cancer treatment but it is still widely used and highly effective, and well-established as a cancer treatment. However its safety profile makes it unfavorable. Plinabulin, combined with docetaxel, mitigates the safety concern of neutropenia.

"The addition of plinabulin adds to overall efficacy by firstly keeping a higher number of patients at a high docetaxel dose. Then in addition to that, plinabulin has direct anti-tumor effects and immune-enhancing effects."

Along with the NSCLC and neutropenia programs, plinabulin has entered clinical trials in combination with nivolumab and it is likely to be tested in other oncology studies.

As well as that, BeyondSpring also has additional next-generation immuno-oncology candidates and a technology platform for targeted drugs and at least six new development compounds per year through a recently established five-year research collaboration with the USA's Fred Hutchinson Cancer Research Center.

"Our company has a strong focus on innovation but also a strong development strategy combining resources and capabilities in the USA with those in China," Dr Mohanlal says.

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