BeyondSpring CEO Reveals Novel Tumor Therapy

The company is working on regulatory approvals in the U.S. and China.

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TheStreet Video

New York-based BeyondSpring develops oncology products with Plinabulin, a small molecule that attacks tumors and can activate the Rho guanine nucleotide exchange factor GEF-H1, which could play a role in managing a variety of diseases.

Research has found a wide array of related therapies.

Research has confirmed "the roles of GEF-H1 in epithelial barrier permeability, cell motility and polarization, dendritic spine morphology, antigen presentation, leukemic cell differentiation, cell cycle regulation, and cancer," according to the National Health Institutes' NCBI.

"GEF-H1 might also contribute to pathophysiological signaling involved in leukemias, and in cancers associated with mutated p53 tumor suppressor gene, epithelial and endothelial cell dysfunction, infectious disease, and cardiac hypertrophy. We suggest that GEF-H1 could be a novel therapeutic target in multiple human diseases."

The p53 tumor suppressor gene may not always actually suppress tumors, but its manipulation remains a focus of medical research.

BeyondSpring has Plinabulin in clinical trials for the treatment of conditions including neutropenia and non-small cell lung cancer (NSCLC). Pre-clinical trials are developing applications for metastatic brain tumor.

Neutropenia is a condition involving an abnormally low count of neutrophils, which help fight off illnesses—particularly those caused by bacteria.

Co-founder, chairperson and CEO Lan Huang provided The Deal, the sister publication of TheStreet, with a look at Plinabulin and how testing drugs in China works in conjunction with the Food and Drug Administration.

Huang previously co-founded Wuxi MTLH Biotechnology Co. Ltd., which was acquired by Shanghai Pharmaceutical Group in 2010, and Paramax International, which was acquired by RPS, then sold to Warburg Pincus in 2011.

Huang and the company's CSO, CRO and CMO all have doctorates in scientific specialties, and the CMO has M.D. and M.B.A degrees as well. It's not a company managed purely by licensers.

"We are now venturing deep into immuno-oncology (I/O) combinations of Plinabulin," Huang told The Deal.

"There are more than 1,000 I/O combinations that aim to increase the efficacy of checkpoint inhibitors—but so far, no other combinations are also aimed at reducing checkpoint inhibitors' immune-related severe adverse effects (SAE), which could prevent patients from taking these agents.

Checkpoint inhibitors are drugs that can help immune systems to respond to threats more efficiently

"Plinabulin is a unique agent with the potential to not only increase efficacy—by activating dendritic cell maturation, which leads to T-cell activation—but also to reduce immune-related SAEs by inhibiting PDE activities," Huang said.

"From our preliminary data, in 10 patients who received Plinabulin in combination with Nivolumab, none experienced immune-related SAEs. Now, we are implementing triple I/O combinations with Plinabulin to further evaluate Plinabulin's effects."

Nivolumab is a drug used to treat cancer under specific genetic conditions involving the B-Raf gene, which can cause cancer under some mutagenic conditions.

The company continues to work within both U.S. and China regulatory frameworks.

"We plan to conduct one global Phase 3 trial in the U.S. and China, as well as in other Western counties, and combine the data for a New Drug Application (NDA) filing in the U.S. and China," Huang said.

"We use the same protocol for each indication that is approved by the U.S. Food and Drug Administration (FDA) and China FDA (CFDA). We also use one global clinical CRO [Contract Research Organization] to enroll patients and a global central lab to ensure that all PK, efficacy and safety profiles of patients from all regions are similar so that the data can be combined for filing."

BeyondSpring is working on two applications in both countries.

"With the recent reforms in the CFDA regulations, Plinabulin has the distinct privilege to be able to file for NDA in China for both Phase 3 indications—chemotherapy-induced neutropenia (CIN) prevention and non-small cell lung cancer (NSCLC) treatment—as early as late 2018 or early 2019, provided that the data shows a clinical efficacy trend. In the U.S., we are still on track to file for NDA for the CIN indication in 2019 and for the NSCLC indication in 2020."

Plinabulin is distinct from the PD-1 antibody.

PD-1, or programmed cell death protein 1, keeps the immune system in check but can sometimes limit responses to aggressive immune system threats.

"Using a car as an analogy for the I/O effects in the body, the PD-1 antibody releases the brakes on the car—letting T-cells see cancer cells—while Plinabulin adds 'fuel' into the car—inducing dendritic cell maturation—leading to downstream T-cell activation," Huang said.

"Thus, the two of them together can help to accelerate the car to run faster."

BeyondSpring went public in March 2017 with a combined initial public offering and private-investment-in-public-equity offering.

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