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With an Immuno-Oncology Drug in Phase 3 Trials for Non-Small Cell Lung Cancer, Phase 2/3 Registration Trial for Preventing Neutropenia and Business Model Integrating U.S. and China Resources, BeyondSpring is Well-Positioned for Growth

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CEOCFO: ***Dr. Huang, what is the concept for BeyondSpring?***
Dr. Huang: BeyondSpring is a global clinical stage biopharmaceutical company focused on immuno-oncology treatments. We have a robust pipeline from internal development and from our research agreements with institutions such as the Fred Hutchinson Cancer Research Center (FHCRC) and University of Washington. Our lead compound, Plinabulin, is already in two global Phase 3 trials: one for non-small cell lung cancer, and the other is a Phase 2/3 registrational trial for the prevention of Neutropenia.

CEOCFO: ***Would you tell us about Plinabulin? How does it work, what does it do and what is the science behind it ?***
Dr. Huang: Plinabulin is an immune-enhancing mechanism agent, which activates the dendritic cell maturation and leads to T-cell activation. With this activity, it has anti-cancer effects, such as in non-small cell lung cancer. It also has a Neutrophil protection function, which, in fact, led to the prevention of Neutropenia indication.

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CEOCFO: ***Has this approach been tried before? What is different about how your drug works as opposed to other therapeutic approaches or what might be available today?***
Dr. Huang: We have a very different way of treating cancer. From an anti-cancer point of view, Plinabulin is a small molecule immuno-oncology agent, rather than a large molecule immuno-oncology agent. It is very different from PD-1 antibodies, which release the brake of the immune system so that the T-cell can see the cancer cells. Instead, Plinabulin is adding the fuel to the car, basically adding T-cells into the system to kill cancer. That is how it is differentiated in its mechanism for the anti-cancer effect.

Plinabulin is also currently in a Phase 2/3 registration trial for the prevention of Neutropenia, which is an abnormally low blood concentration of Neutrophils, a type of white blood cell. Neutropenia represents a key limitation that's associated with most chemotherapy. The current treatment in that indication is G-CSF (granulocyte colony stimulating factor), which works on bone marrow and releases the Neutrophil. Plinabulin works differently, as it protects the Neutrophil from breakdowns. With this different mechanism, Plinabulin has less than 4 percent bone pain, whereas G-CSF has over 20 percent bone pain. Plinabulin also has highly statistically significant data in the efficacy of reducing severe chemo-induced Neutropenia.

CEOCFO: ***What surprised you so far through the process and through the trials?***
Dr. Huang: We have two global registrational trials that are ongoing, based on Plinabulin's Phase 1/2 data in over 140 patients. What we have found in the anti-cancer indication is that Plinabulin, when combined with Docetaxel, has a really long overall survival benefit: 11.3 months versus 6.7 months for Docetaxel alone. Therefore, it has a benefit of 4.6 months. We also see the response rate in the combination to be 18.4 percent versus 10.5 percent in Docetaxel alone, so it is almost doubling Docetaxel's effect. That is a really dramatic improvement. In addition, we also see the Neutropenia reduction benefit, which is very surprising from our Phase 2 data, because if you put two small molecules together, you usually would not expect the secondary benefits. However, because of Plinabulin's immune mechanism, it can protect the Neutrophil from breaking down, and that is why we see this dramatic reduction in Neutropenia in our Phase 2 trial.

CEOCFO: ***Would you tell us about some of your other drugs in the pipeline?***
Dr. Huang: Plinabulin is actually the main pipeline drug, so we have these two global registration trials with lung cancer and the prevention of Neutropenia. In addition, we also have a Phase 1/2 Nivolumaub combo trial with Plinabulin at the University of California, San Diego, and Fred Hutchinson Cancer Research Center. That is really at the forefront of immunotherapy combinations, and this data will be coming out within a year, which is very exciting. In addition, Plinabulin can also work in KRAS mutants and brain tumors, and for those two indications, there are no approved drugs on the market. Therefore, Plinabulin's potential effectiveness in those indications actually could be very exciting.

Besides Plinabulin, we also have a strong pipeline. From our internal development, we have assets BPI-002, BPI-003 and BPI-004, which induces T-cell activation, acts as an IKK inhibitor and focuses on a small molecule that induces the production of antigens by tumor cells, respectively. Our research agreement with Fred Hutchinson and the University of Washington will give us additional compounds. The first platform that we are currently working on is called the ubiquitin degradation pathway, which will give us a great number of candidates in the future.

CEOCFO: ***Would you tell us about your business model, integrating US and Chinese clinical resources? How is it effective?***
Dr. Huang: With this integration model, we can contribute time- and cost-efficiency in drug development. For example, in our current non-small cell lung cancer trial, we are enrolling 80 percent of the patients in China versus 20 percent of the patients in the U.S. and other counties. This brings cost- and time-savings, because China has over 700,000 lung cancer patients, while the U.S. has only 200,000. In China, the majority of cancer patients enroll in clinical trials. In addition, the cancer centers are located in central locations, such as Beijing, Shanghai and Guangzhou, so you can enroll patients very fast. For example, one drug called Afatinib, which is approved by the U.S. FDA, had 72 percent of patients from China for its pivotal trial, and it enrolled 240 patients in six months. Another lung cancer drug, Icotinib, enrolled 400 patients in China in nine months, which is also dramatic.

On the contrary, in the U.S., sometimes only 4 to 6 percent of patients enroll in clinical trials, and there are over a few hundred trials that are competing at any given time, which is why it is very slow to enroll patients in the U.S. In terms of cost efficiency, in China, each patient costs between one-third to one-fifth of the U.S. cost, so if we enroll 80 percent of our patients from China, then that really adds to our overall cost benefit. We have this competitive advantage, because our company has soldiers on the ground in China, where we have an office in Dalian. Therefore, we have people who will help to oversee the trials according to U.S. GCP. In addition, it was my honor to receive the Thousand Talent Innovator Award from the Chinese President, so the innovative drug projects that I lead, including BeyondSpring's work with Plinabulin, move into fast track review with the Chinese government. That gives us additional speed in the regulatory arena in China. All of this combined gives our company a specialty of time- and cost-efficiency, which is a disruptive business model.

CEOCFO: ***Has the medical community been paying attention? Do they understand what you are doing?***
Dr. Huang: Recently, on Feb. 23, 2017, we gave an oral presentation at ASCO-SITC, the first immuno-oncology symposium of ASCO, which represents the highest distinction of clinical data in the oncology field. In the daily news at

ASCO-SITC, we were ranked the No. 1 project of the five highlighted projects there. This is for the anti-cancer indication of Plinabulin for lung cancer. In addition, we were invited to give a presentation at the ASH conference, which happened in December 2016 in San Diego, and that was for the Neutropenia prevention indication. Those are the conferences with clinicians from the highest levels of distinction. For our trials, we also attract industry KOLs to run them; for example, for the Neutropenia prevention indication, Dr. Douglas Blayney, Professor of Medicine (Oncology) at Stanford University, is running our Phase 2/3 trials. He was also a participant of the Neulasta trial before, so he understands the area and is a well-respected figure in Neutropenia management. He is a board member of the National Comprehensive Cancer Network (NCCN) and contributor to the NCCN guidelines for Neutropenia management. We are very lucky that he supports our program and is helping to run it.

CEOCFO: ***How do you stay focused as CEO with so many things going on both from the business side and from the development and the pipeline?***
Dr. Huang: For me, I am a scientist-turned-entrepreneur, with a Ph.D. from UC Berkeley. I was also a research fellow at the Memorial Sloan Kettering Cancer Center and published in both *Science* & *Nature*. Therefore, I have very strong training in science and experience in the development and research arena. I understand it all very well, and I love what I do. I love to translate the discoveries from the bench side to the bed side, and that is why I can manage this biotech company. On the business side, since 2002, I have been an entrepreneur, with BeyondSpring being my fourth company, so I understand the business behind a biotech corporation. What I am doing at BeyondSpring is integrating the science and business to maximize value for our shareholders.

CEOCFO: ***Why pay attention to BeyondSpring Pharmaceuticals, from both the medical side and from the investment side?***
Dr. Huang: From the medical side, our lead asset, Plinabulin, is a really exciting compound, because this agent has an immune-enhancing mechanism and is currently in two global registration trials: one in lung cancer, and it is very differentiated from other agents in this treatment area. In addition, in the prevention of Neutropenia, it is also very differentiated from G-CSF. From the patient point of view in the clinic, our drug is really well-differentiated and can help many people in the future. From an investment point of view, we have a disruptive and differentiated R&D model, which integrates U.S. and China resources to contribute time- and cost-efficiency into innovative development. That eventually will help to drive down the pricing issue of innovative drug development.