BeyondSpring Presents Lead Asset's Mechanism Data for Prevention of Chemotherapy-Induced Neutropenia

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NEW YORK – APRIL 17, 2018 – BeyondSpring Inc. (NASDAQ:BYSI), a global, clinical-stage biopharmaceutical company focused on the development of transformative cancer therapies, today announced the presentation of preclinical data from the Company's lead asset, Plinabulin, at the American Association for Cancer Research (AACR) Annual Meeting, being held on April 14-18, 2018, at McCormick Place in Chicago. The preclinical data will be presented in a poster titled, "Plinabulin ameliorates chemotherapy-induced neutropenia: Mechanistic insights," from 1:00 to 5:00 p.m. CDT at the McCormick Place North / South Exhibit Hall (Poster Session 37, Abstract No. 4805 / 4). The data demonstrate Plinabulin's novel mechanism in preserving neutrophil (a type of white blood cell) amount in bone marrow after docetaxel treatment, a mechanism that is differentiated from that of G-CSF, which is the current standard of care, in the prevention of chemotherapy-induced neutropenia (CIN).

The preclinical study evaluated Plinabulin's role in regulating neutrophil biology and docetaxel CIN. Mice were intravenously treated with a single injection of docetaxel at 25 mg/kg, with and without Plinabulin at 10 mg/kg or 20 mg/kg, into the abdominal cavity, one hour later. The Plinabulin 10 mg/kg in mice corresponds to dose levels in humans that are used in our current clinical trials. Complete blood counts (CBC) were performed at three, four and five days post-injection, with bone marrow analysis after five days.

Plinabulin significantly reduced docetaxel-induced neutropenia at Day Five ($p<0.05$) in this mouse study. Bone marrow neutrophil counts were decreased by docetaxel monotherapy, but reduction in bone marrow neutrophil counts was prevented when Plinabulin was administered with docetaxel (for Plinabulin at 10 mg/kg, $p<0.001$; for Plinabulin at 20 mg/kg, $p<0.01$). The docetaxel-induced accumulation of uncommitted hematopoietic stem cells (LSK cells) was significantly prevented by Plinabulin, and Plinabulin's effect appeared to be neutrophil-specific; Plinabulin had no effect on monocytes. Collectively, these data suggest that Plinabulin reduces CIN by protecting the normal transition of LSK to myeloid precursors in mice (which is arrested by docetaxel alone) and represent a novel mechanism for the prevention of CIN.

CIN is a common side effect of many cancer chemotherapies that results from the absence of neutrophils, which are critical in the defense against infections. Cancer patients who develop CIN are more susceptible to severe and life-threatening infections, may have their chemotherapy treatment reduced or interrupted and may require hospitalization.

The current standard of care in the prevention of CIN is G-CSF (granulocyte colony stimulating factor), which has important limitations: G-CSF causes medullary bone pain, as it stimulates the

expansion and proliferation of neutrophil precursors in the central part (or medullary compartment) of bone marrow. This medullary or expansive bone pain is peculiar to conditions in which the bone marrow is extremely active. Furthermore, G-CSF must be administered 24 hours or more after the chemotherapy infusion (per the approved label). Thus, there is an unmet medical need for patients who suffer from CIN.

"The mechanistic data presented today validate the clinical data observed to date demonstrating that Plinabulin may produce less bone pain versus Neulasta in patients with CIN," said Dr. Klaus Ley, senior author, professor at La Jolla Institute of Allergy and Immunology and expertresearcher in the field of neutrophil biology for 30 years. "As shown in this study, Plinabulin preserved neutrophil counts not by stimulating neutrophil production, but by protecting existing neutrophil precursors. Thus, I would not expect Plinabulin to provoke expansive bone pain. Furthermore, in BeyondSpring's CIN 105 Study, Plinabulin was administered as soon as 30 minutes after docetaxel chemotherapy. I believe that Plinabulin's product profile has potential advantages over G-CSF – an area that has seen little innovation in the past three decades."

"In prospective clinical studies, Plinabulin has not only produced statistically significant reductions in severe neutropenia induced by docetaxel, but it can also be administered 30 minutes to one hour following chemotherapy and has been associated with less bone pain – two limitations associated with G-CSF," added Dr. Lan Huang, BeyondSpring CEO. "Today's mechanistic data give a scientific foundation that supports what we believe could be a unique and innovative option for preventing CIN. We look forward to late-stage clinical data from ongoing head-to-head trials testing Plinabulin versus Neulasta this year."

Plinabulin is BeyondSpring's lead clinical asset currently in global registrational studies for the prevention of CIN and treatment of NSCLC. Under BeyondSpring's dual-market strategy, Plinabulin's global development program is designed to support New Drug Application (NDA) submissions in China and the U.S. BeyondSpring plans to submit the first of these to the China Food and Drug Administration (CFDA) in the fourth quarter of 2018 or early 2019 for a CIN indication, and in the first half of 2019 for an indication in NSCLC, subject to positive results from its ongoing late-stage studies. The U.S. NDA is planned for submission in 2019 for the CIN indication and in 2020 for NSCLC.

About Chemotherapy-Induced Neutropenia (CIN)

CIN is a common side effect in cancer patients that involves the destruction of a type of white blood cell (neutrophil), a patient's first line of defense against infections. Patients with severe, or grade 4 neutropenia have an abnormally low concentration of neutrophils, making them more susceptible to severe bacterial and fungal infections and sepsis, requiring hospitalization. When severe neutropenia occurs, the chemotherapy dose has to be reduced or interrupted until the neutropenia subsides. More than 60,000 patients are hospitalized each year for CIN in the U.S., which sometimes results in death. The severity of neutropenia is measured by DSN, which

measures the days a patient has a dangerously low neutrophil count. DSN of less than one day is considered clinically meaningful.

The current standard of care for prevention of CIN is G-CSF, which accelerates maturation and proliferation of neutrophil precursors, and, when administered the day after chemotherapy, reduces DSN of docetaxel to less than one day. G-CSF has the limitation of second-day dosing after chemotherapy treatment and bone pain in 10 to 29 percent of patients, with some patients citing bone pain as “excruciating.” For the intermediate-risk chemotherapy market, which represents 60 percent of cases, National Comprehensive Cancer Network (NCCN) guidelines recommend G-CSF treatment only in limited, patient-specific circumstances.

Global sales of G-CSF totaled more than $8 billion in 2016, with the current G-CSF market leader, Neulasta, contributing approximately $6 billion. In the U.S., Neulasta sales totaled more than $4 billion in 2016.

About Plinabulin
Plinabulin, a marine-derived small-molecule, is BeyondSpring’s lead asset and is currently in late-stage clinical development for the prevention of docetaxel chemotherapy-induced neutropenia (CIN) and as an anticancer therapy in non-small cell lung cancer (NSCLC). Studies of Plinabulin's mechanism of action indicate that Plinabulin activates GEF-H1, a guanine nucleotide exchange factor. GEF-H1 activates downstream transduction pathways leading to the activation of the protein c-Jun. Activated c-Jun enters the nucleus of dendritic cells to up-regulate immune-related genes, which contributes to the up-regulation of a series of genes leading to dendritic cell maturation, T-cell activation and other effects that prevent neutropenia by reducing the neutrophil breakdown.

About BeyondSpring
BeyondSpring is a global, clinical-stage biopharmaceutical company developing innovative immuno-oncology cancer therapies with a robust pipeline from internal development and from collaboration with University of Washington in de novo drug discovery using ubiquitination platform. BeyondSpring’s lead asset, Plinabulin, is in a Phase 3 global clinical trial as a direct anticancer agent in the treatment of non-small cell lung cancer (NSCLC) and two Phase 2/3 clinical programs in the prevention of chemotherapy-induced neutropenia (CIN). BeyondSpring has a seasoned management team with many years of experience bringing drugs to the global market.

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