BeyondSpring Announces Initiation of Phase 3 Clinical Development for Plinabulin for Prevention of Chemotherapy-Induced Neutropenia

First-in-Class Small Molecule Drug Has Potential for Same-Day Dosing, Reduced Bone Pain and Improved Side-Effect Profile Compared to Current Standard of Care

New York, N.Y. – March 19, 2018 – BeyondSpring Inc. (NASDAQ: BYSI), a global, clinical-stage biopharmaceutical company focused on the development of transformative cancer therapies, today announced that the Company has initiated the Phase 3 portion of Study 105 evaluating its lead asset, Plinabulin, for the prevention of chemotherapy-induced neutropenia (CIN) associated with docetaxel, a cytotoxic chemotherapeutic. CIN is a common side effect of many cancer chemotherapies, and results from the destruction of neutrophils (a type of white blood cell that is critical in defense against infections). Cancer patients who develop CIN are more susceptible to severe and life-threatening infections, may have to have their chemotherapy treatment reduced or interrupted, and may require hospitalization. The Study Initiation meeting was held in Dalian, China with the BeyondSpring team, CIN global Principal Investigator Dr. Douglas Blayney and more than 70 clinical investigators and supporting staff.

Dr. Blayney, Professor of Medicine at Stanford University, noted, "There have been minimal advancements in the treatment of CIN in the past 30 years, and patients will benefit from new approaches that can overcome the limitations associated with current practice. The goal of neutropenia therapy is to reduce potentially life-threatening infections associated with chemotherapy. Reducing the duration of severe neutropenia (DSN), which lowers the amount of time chemotherapy patients are at infection risk, predicts patient benefit. Reduction of DSN to less than one day is clinically meaningful. **In the Phase 2 portion of Study 105, Plinabulin achieved the target DSN reduction**."

The current standard of care for CIN is G-CSF, which accelerates maturation of neutrophils and increases proliferation and expansion of neutrophil precursors in the bone marrow. While G-CSF reduces DSN, it cannot be given on the same day as chemotherapy, and the expansion of the bone marrow causes an unusual bone pain in 10 to 29 percent of patients. This unusual, expansive bone pain causes some patients to discontinue treatment. Because of Plinabulin's novel mechanism of action, this expansive bone pain has not been observed in previous clinical studies (non-small cell lung cancer or NSCLC Study Study 100 and Study 101). In the Phase 2 portion of Study 105, a single dose of Plinabulin, 30 minutes after docetaxel, demonstrated similar efficacy relative to long-acting G-CSF (Pegfilgrastim/Neulasta) dosed the next day in the first 21-day cycle (the primary efficacy endpoint). The study achieved its primary objective in identifying the recommended Phase 3 dose (20 mg/m^2) with a clear dose-dependent response; DSN is 0.38 days for Plinabulin at 20 mg/m^2. This data was presented at the 2018 ASCO-SITC Clinical Immuno-Oncology Symposium in January. Plinabulin has also demonstrated anti-cancer activity in Study 100 and Study 101 and is now in Phase 3 clinical development for the treatment of NSCLC (Study 103).

The Phase 3 portion of Study 105 is expected to enroll approximately 150 cancer patients at 55 sites in the U.S., China, Ukraine, Russia and Hungary. Patients will be randomized to receive either Neulasta or Plinabulin. The protocol provides for an interim analysis after 100 patients have been dosed after first cycle of chemotherapy. The primary endpoint of Study 105 is the reduction of neutropenia, measured by DSN, in the first cycle. Secondary endpoints include the incidence of neutropenia, incidence of febrile neutropenia, incidence of and duration of hospitalization, and incidence of bone pain, among others.

"In the Phase 2 portion of Study 105, more than 50 patients were enrolled in six weeks among 40 sites globally. We are excited to advance this study and look forward to providing Phase 3 interim data in the second half of 2018," said Dr. Ramon Mohanlal, Chief Medical Officer at

BeyondSpring. “If the Phase 3 DSN data is consistent with the data from the Phase 2 portion, we would view the trial as successful. Together with data from the overall CIN development program and safety data from NSCLC Study 101 and Study 103, we believe this would form the basis for a new drug application submission for CIN to the China Food and Drug Administration (CFDA) in late 2018 or early 2019.”

“Initiating the Phase 3 portion for Study 105 with Plinabulin for CIN prevention is a major milestone for BeyondSpring. We believe that a significant reduction in the DSN endpoint, together with a manageable safety profile, would support a successful new drug application for CIN in the US and globally,” concluded Dr. Lan Huang, CEO of BeyondSpring. “A successful outcome could position Plinabulin to address the majority of high-risk chemotherapy cases, as well as the underserved intermediate-risk chemotherapy patient population.”

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 or white blood cells, making them more susceptible to severe bacterial, viral and fungal infections and sepsis, which require 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., resulting in death in up to 18 percent of these cases. The severity of neutropenia can be measured by DSN, which measures the days a patient is in a hospital due to low white blood cell count. DSN of less than one day, or hospitalization 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 Neulasta selling around $6 billion. In the U.S., Neulasta sales totaled more than $4 billion in 2016.

About Registration Program for CIN
As part of the Company’s registration program for Plinabulin in the treatment of CIN, Plinabulin is currently being studied in two Phase 2/3 clinical trials for the reduction of intermediate risk chemotherapy docetaxel CIN (Study 105) in NSCLC, breast and prostate cancer, and for the reduction of high risk chemotherapy TAC CIN (Study 106) in breast cancer patients. The Phase 2 portion of Study 105 enrolled 55 NSCLC patients and Plinabulin when dosed once, 30 minutes after docetaxel, was shown to prevent CIN and established the recommended Phase 3 dose. The Phase 3 portion of Study 105 is expected to enroll approximately 150 patients with NSCLC, breast or prostate cancer. The Phase 2 portion of Study 106 is enrolling approximately 60 patients and is expected to be completed in 2018; and phase 3 portion is expected to enroll approximately 120 patients. Additionally, in Study 103, a Phase 3 trial in the United States, China and Australia of Plihabulin in combination with docetaxel in patients with advanced NSCLC, data from 138 patients on a secondary endpoint of grade 4 neutropenia reduction, prospectively demonstrated Plinabulin’s ability to reduce docetaxel grade 4 neutropenia in NSCLC patients ($p<0.0001$). These three trials are expected to form the efficacy dataset for the NDA filings for Plinabulin in CIN.

Based upon the Company's discussions with the China regulatory authorities or CFDA, the Company believes its registration program for Plinabulin in CIN meets the criteria for accelerated approval of a novel drug for a life threatening diseases based upon clinical efficacy trend data and that the efficacy data from both the interim data of the phase 3 portion of Study 105 and the data from the phase 2 portion of Study 106 expected in 2018, if positive, will be sufficient to demonstrate the requirements for such a trend and therefore the Company expects to file its China NDA for CIN in late 2018 or early 2019.

About Plinabulin

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. To reduce CIN, Plinabulin is given as a single intravenous infusion in each cycle, 30 minutes to 1 hour after completion of the chemotherapy, offering same-day dosing, whereas G-CSF is given 24 hours after chemotherapy. Plinabulin has also demonstrated anti-cancer activity in a 163-patient, global Phase 2 study of patients with non-small cell lung cancer (NSCLC), study 101. In addition, the use of Plinabulin is associated with little bone pain as shown in NSCLC Study 100 and Study 101, which is a frequent side effect with G-CSF.

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 clinical trial as a direct anticancer agent in non-small cell lung cancer (Study 103) and two Phase 2/3 clinical programs in the prevention of chemotherapy-induced neutropenia (CIN) – (Studies 105 and 106). BeyondSpring has a seasoned management team with many years of experience bringing drugs to global market.

Cautionary Note Regarding Forward-Looking Statements

This press release includes forward-looking statements that are not historical facts. Words such as "will," "expect," "anticipate," "plan," "believe," "design," "may," "future," "estimate," "predict," "objective," "goal," or variations thereof and variations of such words and similar expressions are intended to identify such forward-looking statements. Forward-looking statements are based on BeyondSpring's current knowledge and its present beliefs and expectations regarding possible future events and are subject to risks, uncertainties and assumptions. Actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of several factors including, but not limited to, the anticipated amount needed to finance the Company's future operations, unexpected results of clinical trials, delays or denial in regulatory approval process, our expectations regarding the potential safety, efficacy or clinical utility of our product candidates, or additional competition in the market. The forward-looking statements made herein speak only as of the date of this release and BeyondSpring undertakes no obligation to update publicly such forward-looking statements to reflect subsequent events or circumstances, except as otherwise required by law.

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Media Relations:
Caitlin Kasunich / Kathryne Hunter
KCSA Strategic Communications

212.896.1241 / 212.896.1204
ckasunich@kcsa.com / khunter@kcsa.com

Investor Relations:
Laura Perry or Joe Rayne
Argot Partners
212.600.1902
BeyondSpring@argotpartners.com