



BeyondSpring Announces Positive Topline Results from its DUBLIN-3 Registrational Trial of Plinabulin in Combination with Docetaxel for the Treatment of 2nd/3rd Line Non-Small Cell Lung Cancer (NSCLC) with EGFR Wild Type

- *Study met primary endpoint showing statistically significant improvement in overall survival (OS) for the combination vs. docetaxel.*
- *Study met key secondary endpoints showing statistically significant improvement for the combination against docetaxel alone in ORR, PFS, and 24- and 36-month OS rates, and significant reduction in incidence of Grade 4 neutropenia.*
- *BeyondSpring plans to seek U.S. FDA and China NMPA approval for plinabulin in combination with docetaxel in NSCLC based on the demonstrated clinical benefit and safety profile.*
- *Full data is planned to be presented at upcoming medical conference; The company will host a call at 8:30 a.m. ET today. Dial-in: 877-451-6152, conference ID# 13722298*

NEW YORK, August 4, 2021 (GLOBE NEWSWIRE) -- BeyondSpring (the "Company" or "BeyondSpring") (NASDAQ: BYSI), a global pharmaceutical company focused on the development of cancer therapeutics, announced today the positive topline data of DUBLIN-3 registrational trial in plinabulin in combination with docetaxel to treat 2nd and 3rd line NSCLC (EGFR wild type) compared to docetaxel alone (n=559). Plinabulin is a first-in-class, *selective immunomodulating microtubule-binding agent (SIMBA)*, which is a potent antigen presenting cell (APC) inducer. The data released today showed that compared to docetaxel alone, the combination met the primary endpoint of increasing overall survival (mean OS, p = 0.03; OS log rank, p <0.04) and met key secondary endpoints, including significantly improving ORR, PFS and 24- and 36-month OS rates, and significant reduction in the incidence of Grade 4 neutropenia.

The DUBLIN-3 Phase 3 trial is a randomized, single blind to patients, active controlled, global trial that enrolled 559 patients in 2nd and 3rd line NSCLC, EGFR wild type, with measurable lung lesion. Patients were treated on a 21-day cycle with infusion of docetaxel (75 mg/m² on day 1) and plinabulin (30 mg/m² on days 1 and 8) vs. docetaxel alone (75 mg/m², day 1). The primary endpoint was overall survival. Plinabulin in combination with docetaxel (DP) showed statistically significant improvements compared to docetaxel alone (D) with topline data summarized below for ITT population (DP: n=278; D: n=281).

- Primary endpoint (Overall Survival):
 - o mean OS: p=0.03; OS log rank: p<0.04
- Key secondary endpoints:
 - o ORR (p<0.03)
 - o PFS (p<0.01)
 - o Incidence of Grade 4 neutropenia, cycle 1 day 8 (DP: 5.3% vs. D: 27.8%; p<0.0001)
 - o 24 Month OS rate (DP: 22.1% vs. D: 12.5%; p <0.01)
 - o 36 Month OS rate (DP: 11.7% vs. D: 5.3%; p = 0.04)
 - o 48 Month OS rate (DP: 10.6% vs. D: 0%; p value cannot be calculated)
- Safety data:
 - o Lower Grade 4 AE frequency and a shift to lower grade AE
 - o No unexpected AE concerns were identified



Trevor M. Feinstein, M.D., of the Piedmont Cancer Institute and a principal investigator for DUBLIN-3 commented, “The treatment of 2nd and 3rd line NSCLC, especially with EGFR wild type where tyrosine kinase inhibitors do not work, is an area of severe unmet medical needs. Now that checkpoint inhibitor immunotherapy has moved into first line, there is a vacuum in this indication, where treatment is heavily centered around docetaxel. Currently, docetaxel-based therapies have limited survival benefit and >40% severe neutropenia. In DUBLIN-3, a prolonged survival benefit, characterized by a long-tailed OS curve, was observed with plinabulin that represents an immune associated anti-cancer benefit. The opportunity that plinabulin offers to these patients is not only to live longer, but also with significantly reduced severe neutropenia, which are both meaningful for these very sick patients.”

Yan Sun, M.D., co-founder and former Chairman of Chinese Society of Clinical Oncology (CSCO), Chairman of NCCN Guidelines of NSCLC in China, and Director of GCP Center at Cancer Hospital of Chinese Academy of Medical Sciences added, “DUBLIN-3 is a pivotal study which succeeded in demonstrating OS benefit for the first agent with a novel mechanism – plinabulin – since the 2015 nivolumab approval. It was very rewarding to be the global Principal Investigator throughout the 6 years for the DUBLIN-3 trial that serves to address this severe unmet medical need. In the DUBLIN-3 study, it is especially gratifying to see the doubling of 24- and 36-month OS rate with a favorable safety profile in the plinabulin combination arm; this profile not only significantly advances NSCLC patients’ care, but also signals plinabulin’s profound immune anti-cancer benefit. The success of the DUBLIN-3 study is the gateway of plinabulin into multiple tumor indications within IO combinations.”

Dr. Ramon Mohanlal, CMO and EVP of R&D of BeyondSpring said, “The success of the DUBLIN-3 study represents proof-of-concept of plinabulin’s immune-enhancing mechanism of action that is complimentary to that of checkpoint inhibitors, and which is the rationale for it to be combined as triple IO combinations in multiple tumor indications. These programs are already in Phase 1/2 stage and preliminary positive results were reported at ASCO 2021.”

Dr. Lan Huang, BeyondSpring’s co-founder, CEO and Chairwoman concluded, “A pre-NDA meeting will be scheduled with the FDA in 2021 to agree on the contents for our NDA, to support a NSCLC indication NDA submission in the first half of 2022. This will be the second indication and second NDA for plinabulin. The superior benefit of plinabulin in reducing severe neutropenia of docetaxel in DUBLIN-3 further supports our first NDA submission in CIN prevention, which received FDA priority review with a PDUFA date of November 30, 2021. Importantly, the strong results from DUBLIN-3 further validate our conviction that plinabulin, as an immune anti-cancer agent, has the potential to be a cornerstone therapy for many solid tumors. I’d like to take the time to thank everyone who helped make this 6-year study run smoothly at more than 60 sites across the U.S., China and Australia, including all participating patients and their families, the investigators and clinical staff and the dedicated BeyondSpring team.”

Conference Call and Webcast Information

BeyondSpring’s management will host a conference call and webcast today at 8:30 a.m. Eastern Time. The dial-in numbers for the conference call are 1-877-451-6152 (U.S.) or 1-201-389-0879 (international). Please reference conference ID: 13722298. A live webcast will be available on BeyondSpring’s website at www.beyondspringpharma.com under “Events & Presentations” in the Investors section. An archived replay of the webcast will be available for 30 days.



About Plinabulin

Plinabulin, BeyondSpring's lead asset, is a *selective immunomodulating microtubule-binding agent (SIMBA)*, which is a potent antigen presenting cell (APC) inducer. It is a novel, intravenous infused, patent-protected, NDA stage asset for CIN prevention and a Phase 3 anti-cancer candidate for non-small cell lung cancer (NSCLC). Plinabulin triggers the release of the immune defense protein, GEF-H1, which leads to two distinct effects: first is a durable anticancer benefit due to the maturation of dendritic cells resulting in the activation of tumor antigen-specific T-cells to target cancer cells, and the second is early-onset of action in CIN prevention after chemotherapy by boosting the number of hematopoietic stem/progenitor cells (HSPCs). Plinabulin received Breakthrough Therapy designation from both U.S. and China FDA for the CIN prevention indication. As a "pipeline in a drug," plinabulin is being broadly studied in combination with various immuno-oncology agents that could boost the effects of the PD-1/PD-L1 antibodies and re-sensitize PD-1/PD-L1 antibody-resistant patients.

About BeyondSpring

Headquartered in New York City, BeyondSpring is a global biopharmaceutical company focused on developing innovative cancer therapies to improve clinical outcomes for patients who have high unmet medical needs. BeyondSpring's first-in-class lead asset plinabulin, is being developed as a "pipeline in a drug." It is filed for approval and has received Priority Review in the U.S. and China for the prevention of chemotherapy-induced neutropenia (CIN) with a PDUFA date of November 30, 2021 in the U.S., and has a fully enrolled pivotal study (DUBLIN-3) to test an anti-cancer benefit with an overall survival primary endpoint in NSCLC. Additionally, it is being broadly studied in combination with various immuno-oncology regimens that could boost the effects of PD-1 / PD-L1 antibodies. In addition to plinabulin, BeyondSpring's extensive pipeline includes three pre-clinical immuno-oncology assets and a subsidiary, SEED Therapeutics, which is leveraging a proprietary targeted protein degradation drug discovery platform.

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, difficulties raising the anticipated amount needed to finance the Company's future operations on terms acceptable to the Company, if at all, unexpected results of clinical trials, delays or denial in regulatory approval process, results that do not meet our expectations regarding the potential safety, the ultimate efficacy or clinical utility of our product candidates, increased competition in the market, and other risks described in BeyondSpring's most recent Form 20-F on file with the U.S. Securities and Exchange Commission. All 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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