



**BeyondSpring Pharmaceuticals Announces Positive Final Phase 3 DUBLIN-3 Data with the Plinabulin/Docetaxel Combination versus Docetaxel Alone in 2nd/3rd Line Non-Small Cell Lung Cancer Patients with EGFR Wild Type at the European Society for Medical Oncology (ESMO) 2021 Congress**

- Study met the primary endpoint showing statistically significant improvement in overall survival (OS) for the combination (DP) vs. docetaxel (D).
- Study met key secondary endpoints showing statistically significant improvement for DP vs. D in ORR, PFS, and 24- and 36-month OS rates, significant reduction in incidence of Grade 4 neutropenia and clinically meaningful relative improvement in Q-TWiST of 18.4%.
- In PD-1/PD-L1 exposed patients, DP had longer OS benefit vs. D (HR = 0.68); and the 24 M OS rate in the combination was triple that of docetaxel (p=0.0026).
- BeyondSpring plans to seek U.S. FDA and China NMPA approval for plinabulin in combination with docetaxel in 2nd/3rd line NSCLC based on the demonstrated clinical benefit and safety profile, with an anticipated NDA filing in 1H 2022.
- More detailed data will be presented live at 8:10 a.m. ET today at the ESMO Congress in Paris, and the Company will host a conference call at 10:00 a.m. ET today. Dial-in: 877-451-6152, conference ID#: 13723041

NEW YORK, September 20, 2021 (GLOBE NEWSWIRE) — BeyondSpring Pharmaceuticals (the “Company” or “BeyondSpring”) (NASDAQ: BYSI), a global pharmaceutical company focused on the development of cancer therapeutics, today will have a late-breaking oral presentation at the European Society for Medical Oncology 2021 Congress. This includes the final intention-to-treat (ITT) dataset from the Company’s DUBLIN-3 Phase 3 registrational trial of its first-in-class lead asset, plinabulin, in combination with docetaxel vs. docetaxel alone for the treatment of 2nd/3rd line non-small cell lung cancer (NSCLC) patients with EGFR wild type. Plinabulin is a *selective immunomodulating microtubule-binding agent (SIMBA)*, which is a potent antigen presenting cell (APC) inducer.

The DUBLIN-3 Phase 3 trial is a randomized, active controlled, single blind to patients, global trial that enrolled 559 patients in 2nd and 3rd line NSCLC, EGFR wild type, with a measurable lung lesion. Patients were treated on a 21-day cycle with infusion of docetaxel (75 mg/m<sup>2</sup> on day 1) and plinabulin (30 mg/m<sup>2</sup> on days 1 and 8) or with docetaxel alone (75 mg/m<sup>2</sup> on day 1). The primary endpoint of OS was met in the ITT population (DP: n=278; D: n=281). The following summarizes the clinical results:

- **Primary endpoint (Overall Survival, ITT population):**
  - o mean OS (SE) months (M): DP 15.08 M (0.848) vs. D 12.77 M (0.676); p=0.0332
  - o median OS (95% CI): DP 10.5 M (9.3, 11.9) vs. D 9.4 M (8.4, 10.7)
  - o Log-rank p=0.0399; HR = 0.82
- **Key secondary endpoints (ITT population):**
  - o ORR (DP: 12.2% vs. D: 6.7%; p=0.0275)
  - o PFS:
    - mean (SE): DP 6.0 M (0.4) vs. D 4.4 M (0.3); p=0.006
    - median (95% CI): DP 3.6 M (3.0, 4.4) vs. D 3.0 M (2.8, 3.7)

- Log-rank  $p=0.008$ ; HR=0.76
  - Incidence of Grade 4 neutropenia, cycle 1 day 8 (DP: 5.3% vs. D: 27.8%;  $p<0.0001$ )
  - 24 Month OS rate (DP: 22.1% vs. D: 12.5%;  $p = 0.0072$ )
  - 36 Month OS rate (DP: 11.7% vs. D: 5.3%;  $p = 0.0393$ )
  - 48 Month OS rate (DP: 10.6% vs. D: 0%;  $p$  value cannot be calculated)
  - Q-TWiST - Quality-adjusted Time Without Symptoms of Disease and Toxicity (DP: 12.40 M vs. D: 10.47 M; 18.43% relative gain in Q-TWiST,  $p=0.0393$ ).
- **Subset Analyses:**
  - PD-1/PD-L1 exposed patients (DP:  $n=62$ ; D:  $n=67$ ; approx. 50% China/50% Western):
    - mean OS (SE): DP 18.33 M (1.909) vs D 13.97 M (1.320);  $p= 0.0602$
    - median OS (95% CI): DP 12.3 M (9.34, 22.88); D 12.1 M (9.76, 13.77)
    - Log-rank  $p = 0.0643$ ; HR = 0.68
    - 24 Month OS rate (DP: 35.8% vs. D: 11.9%;  $p = 0.0026$ )
    - 36 Month OS rate (DP: 12.5% vs. D: 5.0%;  $p = 0.2676$ )
    - 48 Month OS rate (DP: 12.5% vs. D: 0%;  $p$  value cannot be calculated)
- **Safety:**
  - DP is well tolerated, with lower grade 4 and grade 3/4 AE events per patient per year vs. D. 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 (wt) where tyrosine kinase inhibitors do not work, is an area of severe unmet medical need. EGFR wt represents about 85% of Western and about 70% of Asian NSCLC patients. With immunotherapies moved to first line, docetaxel-based therapies are the mainstay therapy here. However, docetaxel-based therapy, although effective, has been known to cause safety concerns such as >40% severe neutropenia and can negatively impact patients’ quality of life (QoL).”

Baohui Han, M.D., Ph.D, Professor, Department of Respiratory Medicine, Shanghai Chest Hospital in China, co-principal investigator of the DUBLIN-3 trial and first author of the ESMO presentation, added, “The DUBLIN-3 data demonstrate that, compared to docetaxel, the plinabulin and docetaxel combination significantly improved treatment efficacy, including extending survival, and significantly reduced severe neutropenia. The >18% gain in Q-TWiST, a measure of survival time spent with good QoL, demonstrated that adding plinabulin to docetaxel led to a clinically meaningful benefit and a favorable benefit/risk ratio. Importantly, in PD-1/PD-L1 exposed patients in DUBLIN-3, the combination showed a more pronounced long-term survival benefit, consistent with the plinabulin immune MOA. Thus, this combination has the potential to be the preferred 2nd/3rd line treatment for NSCLC with EGFR wt.”

Lan Huang, Ph.D., BeyondSpring’s co-founder, chief executive officer and chairwoman, concluded, “When treating advanced cancer, we should focus on improving both the quantity and quality of life for patients, which the plinabulin and docetaxel combination has demonstrated in the DUBLIN-3 study. This study offers clinical evidence that plinabulin could be an important new weapon with a novel MOA in the arsenal that oncologists have to help patients with advanced NSCLC. We’re diligently working to prepare the NDA submission package for this indication in both the U.S. and China and are planning to file these NDAs in 1H 2022. The long-term survival data shown in the DUBLIN-3 study is evidence of the potential of plinabulin’s durable anti-cancer benefit, which we believe will be the gateway for its utility in the triple immuno-oncology combinations in multiple cancer indications, with the potential to help many patients in need.”

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## ESMO Presentation Details

**Title:** A Global Phase (Ph) 3 Trial with the Plinabulin/Docetaxel (Plin/Doc) combination vs. Doc in 2nd/3rd Line NSCLC Patients (pts) with EGFR-wild type (wt) Progressing on a Prior Platinum-Based Regimen

**Session:** Proffered Paper session - NSCLC, metastatic 2

**Date:** September 20, 2021 from 8:10 - 8:20 a.m. ET

**Location:** Channel 4

**Presentation Number:** LBA48

**Speaker:** Trevor Feinstein, M.D., medical oncologist at the Piedmont Cancer Center, Fayetteville, Georgia, USA on behalf of Baohui Han, M.D., Ph.D, Professor in the Department of Respiratory Medicine, Shanghai Chest Hospital, China

## Conference Call and Webcast Information

BeyondSpring's management will host a conference call and webcast today at 10:00 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: 13723041. A live webcast will be available on BeyondSpring's website at [www.beyondspringpharma.com](http://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). It is being developed as a "pipeline in a drug" in multiple cancer indications.

## About BeyondSpring Pharmaceuticals

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" in various cancer indications as direct anti-cancer agent and to prevent chemotherapy induced neutropenia (CIN). Plinabulin and G-CSF combination has filed for approval and has received breakthrough designation and Priority Review in the U.S. and China for the prevention of CIN with a PDUFA date of November 30, 2021, in the U.S. In the DUBLIN-3 study, a global, randomized, active controlled Phase 3 study, the plinabulin and docetaxel combination has met the primary endpoint of extending overall survival compared to docetaxel alone, in 2nd/3rd line NSCLC (EGFR wild type). Additionally, it is being broadly studied in combination with various immuno-oncology regimens that could boost the efficacy of PD-1/PD-L1 antibodies in seven different cancers. 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.

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### **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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